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THE RÔLE OF THE GYNECOLOGIST IN THE FIELD OF CANCER

JANEWAY LECTURE, 1942*

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I WISH that I were able to express to you in words the depths of my gratitude for the honor your Committee has conferred upon me in choosing me to give the Janeway Lecture this year. My appreciation is increased by the conviction that it must have been done as a token of your friendship. May I say with the utmost sincerity that in no other society in which I have had the privilege of membership have I enjoyed more congenial and happy hours.

As I have nothing of scientific value, or bearing upon pure research to offer to you, I have chosen to talk to you about the gynecologist, including his dusty, if not tarnished past, and to endeavor with a crystal glass, which I trust will not be too opaque, to obtain a glimpse of his future, especially where it touches upon our dual fields of radiation and neoplasms.

What is a gynecologist? From whence did he come and whither does he go?

Gynecology means in a broad sense the study of woman. In a narrow sense it refers to the study and consideration of the diseases peculiar to woman.

In many ways these diseases follow or complicate the act of reproduction, which is the greatest act of a woman's life; indeed, is essentially the reason for her existence.

In the earliest times, in all probability, diseases which afflicted the human body were little, if at all, understood and treatment must have been very sketchy. Injuries and accidents of necessity occurred and were taken care of according to the means and judgment at hand.

Childbirth, however, was something whch was a part of the individual and communal life of every tribe and nation. One can readily understand that individuals or groups of individuals by choice or natural aptitude must have set themselves aside to look after and minister to the woman in childbirth. We therefore can find records dating back to the earliest times indicating that special attention was given to the field of obstetrics and that midwifery as a speciality was gradually developed.

There were no books or treatises upon gynecology but there are many publications of great historic interest dealing with the problems and complications of labor and the diseases resulting therefrom. A brief

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reference to these earlier writings may be of some interest.

In 1678, a system of medicine and surgery was published under the supervision and name of Lazarus Riverius. There were seventeen volumes and it contained the writings and opinions of various individuals of that period. The fifteenth volume was devoted to diseases of women and in the preface the author says, "These are called Womens Diseases which are proper to them only, and come from the defect of that part which is distinct in them from men, viz: the womb: of which Democritus in his letter to Hypocrates said, That it was the cause of six hundred miseries and innumerable calamities. All which diseases we shall speak of in as few words as the dignity of the matter will permit." Among the diseases mentioned in this treatise as coming from the cavity of the womb was cancer.

Gynecology continued to be dwarfed by obstetrics or midwifery until the nineteenth century. In fact, such gynecology as there was up to 1850 was chiefly medical gynecology.

When this country was founded in 1776, Gynecology as a Science did not exist. One hundred years later, in 1876, the American Gynecological Society was founded. Its first President, Fordyce Barker, Professor of Clinical Midwifery and Diseases of Women, Bellevue Hospital Medical College, in his annual address ascribed the elevation of this department of Diseases of Women to the rank of a special science as being due to the development of the vaginal speculum and the uterine sound. He said: "The speculum and the uterine probe, by means of which, chiefly, this department of the profession has been raised to the rank of a special science, had been known and probably were used to a limited extent by a few, as they are mentioned by several writers of the seventeenth century: but no allusion to either of these instruments can be found by any writer in the English language, and it is not probable that a single man in England or America ever made use of either of them until within the past half century."

At this first meeting in September, 1876, it is of interest to note that there is in the published transactions not a single reference to cancer, despite the fact that those present were a carefully chosen group, about forty in number, of the most distinguished gynecological specialists in America.

About the time of the organization of the American Gynecological Society the treatment of cancer of any portion of the female generative tract was indeed in a very sad state. In fact, one European writer published an article in 1876 under the title "Gynecological Cancer, noli me tangere." Another writer, Dr. Lever, in a "Prize Essay on Organic Diseases of the Uterus" said regarding cancer of the cervix, "In my opinion it is useless to remove the diseased portion, however favorable the case may be, unless we can remedy the cancerous diathesis which exists in these patients, and which leads to the redevelopment of the disease in the uterus or in some other distant organ." This indicated an attitude of defeatism which I regret to say still exists and is all too common not only in the public mind but among physicians as well. As a matter of fact in the gynecological literature published during that year, 1876, the treatment of cancer of the cervix was limited largely to the use of such substances as chromic acid, nitric acid, chloral hydrate and tincture of eucalyptus. Safe enough for the physician but useless for the patient.

However, in 1809, the surgical world was startled by the first successful abdominal operation for the removal of an ovarian tumor. It was done by Ephraim McDowell in Danville, Kentucky. This operation aroused much discussion and great controversy. From this point onward American physicians rapidly came to the front in the development of the Science of Gynecology.

Indeed, American gynecologists led the way throughout the entire nineteenth century. In 1845 J. Marion Sims devised his operation for the cure of vesicovaginal

fistula. In 1855, largely through Sims' efforts the Woman's Hospital of the State of New York was opened. One of Sims' associates Thomas Addis Emmet, Surgeon to the Woman's Hospital from 1862 to 1900, was a brilliant and gifted gynecologist who developed the field of vaginal plastic surgery as it still is done today. In speaking of the need for surgical repair of obstetrical injuries to the cervix Emmet says, "Much good was accomplished by demonstrating the existence of lacerated cervix and the close relation of the injury to epithelioma, if it be not the actual cause."

In the final quarter of the nineteenth century, gynecological surgeons gradually grouped themselves into special societies in various parts of this country. So rapid was the progress of these men in surgical technique that they led the way not only in their special field but in surgery of the abdomen, and they were pioneers in introducing new surgical methods and procedures. However, the gynecologists met with much sporadic and at times concerted opposition from the general surgeons who endeavored to limit the field of gynecological activity to obstetrics and medical gynecology. This effort, however, was defeated by the establishment in medical schools of separate chairs of gynecology and in various prominent hospitals throughout the country of separate services devoted to the surgical problems of gynecology.

As I have said before, at the time of the Centennial celebration of the founding of this country in 1876, little of value was being accomplished in the treatment of cancer of the female genitals beyond the application of simple medicinal remedies to the ulcerating lesion. At this time a distinguished gynecologist of Brooklyn, New York, John Byrne, was earnestly advocating amputation of the cervix by the galvanocautery as a method of treatment for carcinoma of the cervix. In a paper recording his observations and describing his method in 1877 he wrote as follows: "In conclusion, I have only to say that of all the means and methods thus far suggested or resorted to for amputation of the cervix uteri, whatever conditions indicating or warranting the same may be, galvanocautery will be found to be infinitely the safest, and in the case of cancer particularly, by far the most thorough and radically curative in its tendency." He had then been doing the operation for eight years and among his reported cases already had survivals for six and seven years.

Byrne continued his work and published his results in papers from time to time befor the American Gynecological Society up to 1896. Watkins, in 1915, said that up to that time Byrne's results in the treatment of cancer of the uterine cervix as given in his statistics were the best that had appeared in the transactions of the Society.

Other gynecologists in this country and in Europe followed Byrne's lead in attempting to eradicate cervical cancer by means of the electric cautery, but the number of favorable results on the whole was small and discouraging. As the principles and technique of abdominal surgery, with special reference to hysterectomy, became better defined and the procedure more successfully accomplished, the efforts on the part of the gynecologists to cure cancer of the cervix or body of the uterus by hysterectomy began to accumulate. Despite the development of extensive radical surgical procedures brilliantly conceived and executed by able gynecologists, the end-results of surgery in the treatment of cancer of the cervix at the end of the last century were not satisfactory. Janeway, in 1919, in a splendid report of his personal experience in the treatment of uterine cancer with radium especially commented upon the difficulties the gynecologist experienced at the beginning of the present century in attempting the Wertheim type of radical hysterectomy for cancer of the cervix, as well as the grave risks faced by the patient, for the mortality rates of different operators were high, even though they varied from 10 per cent upwards to 30 per cent. The postoperative morbidity was distressing and

convalescence slow, usually because of urologic complications.

This was the discouraging situation which faced the gynecologist in his effort to cure the most common type of cancer met with in the female generative tract, cancer of the cervix, in the final decade of the last century.

The Gay Nineties famed in song, music, and the drama, as well as for the gorgeous hats—and bustles of the ladies of those years—left a heritage of much joy and laughter for our subsequent entertainment, but all that came out of that decade was as nothing compared with the product of its final years when mankind was blessed by two brilliant scientific discoveries, that of the X-ray by Röntgen in 1895 and radium by the Curies in 1898. The therapeutic possibilities of both the roentgen ray and radium soon were being widely explored both in the laboratory and the clinic.

Among the earliest lesions subjected to treatment by the rays of these two substances were the neoplasms, both benign and malignant, of the female genital tract. With the exception of a New York general surgeon, Robert Abbe, the pioneer work in this field of therapy in America was done, to a large extent, by gynecologists, as well as a few radiologists.

Dr. Howard A. Kelly, at that time Professor of Gynecology at the Johns Hopkins Medical School, and his associate, Curtis Burnam, took up the study and use especially of radium in 1911 and published their first paper on this subject in 1914. From that time onward they held a leading place in developing the entire field of radiation therapy. Other gynecologists of repute and note who rapidly followed their lead were Clark of Philadelphia; Schmitz of Chicago; Lynch of San Francisco, and Bailey of New York. Many others who have come into the field since have done splendid work and reported large numbers of cases successfully treated by either radium or roentgen radiation or a combination of both.

Today the gynecologically trained specialist holds a very prominent place, as a practitioner, as a teacher and an investigator. He has had an extensive preliminary training; not only the academic and professional training required of all medical graduates, but he has spent a greater part of the first five years following his graduation in apprenticeship and study in general and special hospitals in both obstetrics and gynecology. He is a trained diagnostician and surgeon and is fully conversant with the ills that pertain to the human female. The peculiar nature of his work tends to create an atmosphere of intimate confidence and dependence upon him for advice much greater than exists in other branches of medical science. He has an unusual and continuing opportunity to advise and teach his patients on methods and procedures of health, for often his patients are made up in no small number of those whom he has brought into the world and who continue thereafter to seek professional advice from him. He, in my opinion, occupies a position of grave responsibility and great opportunity to work out problems of prophylaxis and cure in his chosen field. It must be assumed that by his special training and education he should be more competent and alert to the danger signals of cancer than many of his associates. Moreover, he should be fully cognizant of the conditions which may be regarded as antecedent to cancer in his particular field. He should also be more conversant with the physiology and pathology, as well as the endocrinology, of the genital tract and breasts than the general surgeon is.

Probably, so far as the broad field of radiation is concerned, the gynecologically trained specialist assumes a very small rôle. Nevertheless, in his own field he must acquire more than a working knowledge of the indications for and application of radiation methods. The need for this knowledge I think is fully recognized today and the younger graduates are to some extent receiving the necessary training and experience to qualify them. Older men should associate such qualified younger men with

them in their work. Individual initiative is worth while but cannot replace good team work.

Referring to radiotherapy, Burnam says: "It is positively certain that the techniques and fields of application of today will not coincide with those of tomorrow. It has become increasingly important, if not an absolute obligation of the gynecologist to thoroughly familiarize himself with these newer tools, and to study their value as applied to his specialty. Only by this means can follow a fruitful coordination of radiotherapy, operative surgery and other methods of treatment."

The family physician, in the final analysis, is the proper person for patients to report to at regular intervals for thorough physical examination. The gynecologist, like other specialists, endeavors to inculcate this thought in the minds of all patients seen by him.

Experience indicates that few patients seek the specialist; the majority consult a general practitioner first and are referred by him to the specialist or expert if he deems it necessary.

The great difficulty is to establish in the public mind the thought that the individual must not wait for symptoms of illness or disease before arranging for the periodic examination.

Cancer in its incipiency in almost any part of the body is a silent disease and as W. S. Stone has well said, "There are no symptoms of beginning cancer and unqualified statements to that effect must be made not only to the public but to the profession."

The educational requirements which a candidate has to meet today in order to be qualified as a specialist in gynecology or obstetrics are on a very high plane, as indeed they are for specialists in radiology and practically every branch of medicine. Their certification by competent examining boards is all in the interests of the public for it requires one who wishes to qualify as a specialist to spend many additional years in study and training after his graduation in medicine.

As I have said before the very nature of the specialty of gynecology and its twin, obstetrics, tends to establish in the minds of patients a sense of confidence and loyalty toward their physician which, on the one hand, encourages and makes it easier for the patient to obey his admonition to report for examination at regular intervals but, on the other hand, it also places a heavy responsibility upon the physician to make sure that his investigation is thorough and that no dull routine or haste enters into it and nothing must be taken for granted. Sins of omission creep in too easily and must be guarded against.

The obligations of the gynecologist to the public, to his fellow physicians and to his patients in the realm of cancer prevention and cure are very great. His opportunities for constructive work in the prevention and cure of cancer as it occurs in the organs peculiar to the female are unbounded. That cancer is the second greatest cause of death in the United States is well known. The total annual toll of deaths is now nearly 160,000. These figures, of course, do not tell us of the additional thousands now ill with cancer who may still be cured if proper treatment is accorded them, nor of the thousands cured each year through early diagnosis, prompt and adequate treatment. Such facts are too little realized and certainly not appreciated, but these facts are far more pertinent than the total of fatalities. For the dead we can do nothing; for the living we must bend every effort to restore them to health.

It is said that 95 per cent of all cancers occur in men and women over thirty-five years of age, and, according to Wilson of the Harvard School for Public Health, more women between the ages of thirty-five to fifty-four inclusive die of cancer than of any other single disease.

Do we as gynecologists realize that 40 per cent of the fatal cancers in women occur in the uterus and breast? I am afraid not. Yet there is not the slightest doubt that three out of four of those patients could

have been cured if the cancer had been recognized in its early stages and efficient treatment promptly instituted. I think it is no exaggeration to say that since the uterus and the breasts are readily accessible to meticulous examination including inspection, palpation and biopsy study it seems that careful checkups every six to nine months would be adequate to give the protection required. In suggesting to our patients the need for such frequent examinations I like to speak, not of the possibility of finding that a cancer has established itself since the preceding visit, but of identifying and curing any and all of the conditions which if neglected may lead to illness or possibly even to cancer; in other words, to keep the patient in such good health that it would be very improbable that cancer would occur. One would think that abnormal bleeding from the genital tract would arouse enough curiosity or anxiety in a patient to cause her to seek immediately the opinion and advice of a physician. Strangely enough, this striking symptom, in fact the only worth while symptom of cancer of the neck or body of the uterus is all too frequently ignored until the disease has become so firmly established and so widespread that the patient is doomed to die. It is a sad commentary on female intelligence that otherwise well women between the ages of forty and fifty years tend to regard any type of abnormal uterine bleeding as significant of the menopause and fail to consult their physician regarding it. We know and they certainly should be told that in many instances the bleeding is caused not by the menopause but by cancer of the neck of the uterus. Due, we believe, chiefly to this mistaken idea and the resulting procrastination, statistics on cancer of the cervix show that fewer women in the menopausal age survive the disease than in the preceding and succeeding decades.

Here, indeed, is a fertile field for the gynecologist to spread the gospel of truth regarding the significance of abnormal uterine bleeding and thereby save countless valuable lives.

Today it would be difficult to speak of the gynecologist in any rôle without referring to endocrines, endocrine organs, hormones and the possible association or influence of these chemical substances upon the development of cancer. This is a pertinent question in view of the extensive and widespread therapeutic use of hormonal products in recent years, especially those obtained from the ovary and testis. The preparations used are given in concentrated form, often parenterally in large dosage and frequently over long periods of time. Moreover, the symptoms for which they are administered occur in the decades of life in which cancer is most commonly met; therefore, one may say in which the predisposition to cancer is greatest. In view of the great influence which the hormones produced by the endocrine organs are known to have upon the entire body and its functions it is not surprising that much study and research have been directed toward investigating a possible relationship between hormones and the development of cancer.

Much has been said on both sides of this subject. The protagonists are those whose chief interest is in animal experimentation whereas the dissenters are the clinicians who deal with human patients. It may be apropos here to quote Rose who says, "The results of animal experimentation are by no means always applicable to the human subject. What is true in the laboratory is not necessarily true at the bedside."

Of all the endocrine organs the ovary is the only one the internal secretion of which has had a definite influence over the growth of cancer in the experimental animal.

Cancer of the cervix and cancer of the breast have been produced in cancer-susceptible strains of male and female mice by large doses of ovarian hormone given over a considerable period of time. It is also known that when ovarian activity is inhibited by removal or destruction of the ovaries, the growth of such spontaneous cancers in mice is retarded. The results of these laboratory experiments in animals are of deep significance to the gynecologist and

clinician and naturally have led to much cautious clinical investigation and study in an effort to check and double check the possibility of similar occurrences in the human subject. However, it should be stated that an amount of estrogen proportionate to that given the experimental animals could not possibly be given to human beings as it would be much too great for human administration. To date there does not seem to be any authentic instance in which cancer in the human has resulted from the administration of ovarian hormone.

Bittner of Bar Harbor made some interesting observations in his experimental studies with foster nursing in cancer-susceptible mice. He found that the incidence of spontaneous cancer in the litter was markedly decreased if the offspring of cancer-susceptible mothers were nursed during the first twenty-four hours of life by mothers of a noncancer-susceptible strain —a remarkable and intriguing observation.

Greene and Brewer, in their interesting study published last year on "Relation of Sex Hormones to Tumors of the Female Reproductive System" said they "do not believe that there is sufficient evidence to clearly establish that any one factor, such as estrogens, is the sole important etiological agent in the production of malignant or non malignant tumors in the human female. There is insufficient evidence available to lead to the assumption that estrogens as produced in the body or as administered by the physician have directly caused tumor formation in the human."

Nevertheless, in view of the importance of this question of estrogenic influence in the inception and growth of human cancer, I would like to quote the following simple precautions advised by Edward Rose, which to me at this time seems sound and logical.

1. Women who have or have had cancer of the breast or any part of the generative system should permanently avoid pregnancy, no matter how completely the cancer seems to have been cured.

2. Women receiving treatment with any of the natural or synthetic ovarian hormones or hormone-like substances over any considerable length of time should have periodic examinations of the breasts and pelvic organs.

3. In accordance with the suggestion of Bittner . . . women with breast tumors or with family histories of such tumors whether benign or malignant should not nurse their daughters at any time.

Finally, I believe that the gynecologist with his knowledge of the anatomy, physiology, pathology and endocrinology of the generative organs should hold himself equally responsible for a similar, thorough knowledge of the problems of the female breasts, as they are too closely related to be dissociated. He should include them in his therapeutic field and should by training, daily contacts and his wide experience with the problems of the female be better qualified to do so than the general surgeon. Many important developments have taken place in gynecology in recent yers and especially can one note a change in many viewpoints.

Dr. Robert L. Dickinson, in referring to gynecologists, said: "Surgery we have promoted. But, if we be just surgeons, by surgeons we may be displaced." Nothing in my opinion could better indicate the need for a full knowledge of the newer concepts of physiology and endocrinology on the part of the specialist surgeon of whom the gynecologist is the one we are discussing as against the mere mechanical performance of operations.

Let us now briefly consider the gynecological cancer field, our successes, our failures and our problems.

Our armamentarium is all-inclusive for we depend upon surgery, radiation, endocrinology, vitamins, oral, parenteral and intravenous administration of various potent drugs, blood and other fluid preparations.

All of these weapons may be brought into play seriatim in a single case before one has exhausted the possibility of cure for the particular patient.

Consider a woman under forty-five years of age with an operable cancer of the breast. The first step is the well recognized

radical surgical removal of the breast with the underlying muscles and all of the axillary lymphatics. Following this, postoperative irradiation with the roentgen ray is utilized for the entire surgical field as a prophylactic measure against local recurrence of the cancer.

In order to permit the patient to withstand the strain of these two major procedures, operation and irradiation, she will receive intravenous medication in the form of glucose and saline solutions, whole blood or blood protein solutions, according to her needs. Vitamins, liver and other chemical preparations will be taken by mouth.

Finally, recourse to endocrine therapy will be had, if she should be unfortunate enough to develop bone metastases. It is now well known that such secondary growth activity can be largely inhibited, the bone lesions caused to regress and indeed be replaced by new bone structure when ovarian secretory activity is terminated; in other words, by destroying the endocrine function of the ovaries. This can be done by surgical removal of the ovaries or it may be adequately accomplished by roentgen castration with less annoyance to the patient.

Similarly, in the treatment of ovarian cancer, it is imperative that all functioning ovarian tissue be removed surgically or destroyed by irradiation.

This does not seem to be fully understood by all who do pelvic surgery, as far too often because one ovary appears grossly to be normal, and the patient is relatively young, still in the menstruating epoch, the surgeon fails to remove the opposite ovary and the uterus.

This usually condemns the patient to the necessity of another operation in a year or less for the cancer rarely fails to develop in the remaining ovary. At the second operation the surgeon seldom finds conditions as favorable for a cure as they were at the first operation.

Such a conservative point of view on the part of the surgeon must be deplored as it indicates a wrong conception of the behavior of ovarian cancer.

One cannot discuss the squamous cancer arising on the skin or mucous membrane of the vulva without referring to Taussig's splendid studies and his reports of surgical cures of this very malignant lesion.

His pioneer work has demonstrated beyond dispute that once the cancer has broken out, the best method of attack is by means of a radical surgical procedure which clears away the vulva with the primary lesion and all of the lymphatic drainage area to and sometimes beyond both groins.

But this is not the heart of the problem. The gynecologist, by his special knowledge, is in a position largely to eradicate this type of cancer by curing the nonmalignant skin lesions of the vulva which almost invariably have been causing severe annoyance to the patient long before the cancer develops.

These skin lesions can be cured by medical means, by endocrine preparations, by irradiation and finally, if necessary, by minor surgical procedures.

The vulva is a great and fertile field for prophylactic gynecologic measures against cancer.

Unless and until the gynecologist and his co-worker, the obstetrician, educate their patients to the thought that by frequent pelvic examinations the physician will be able to recognize and correct, often by office treatment, the common disturbances of the cervix or neck of the womb, such as endocervicitis, erosions, cysts and small tears, nothing worth while will be accomplished in prevention of cervical cancer. And, not many diagnoses of this anatomical site of cancer in its earliest stages will be made. I say this unequivocally and regardless of whether one believes that local injury, infection or inflammation has been satisfactorily demonstrated as the cause of lesions in the cervix that predispose the cervix to cancer. The fact remains that cancer of the uterine cervix, in our statistics, is almost exclusively a disease of married women, nearly all of whom have conceived.

We owe it to these women to do everything in our power as specialists in women's

diseases to protect them from cancer. It seems to me the way is clear and the path not too difficult.

Once the cancer is established in the cervix it is generally conceded that radiation therapy will cure the favorable cases as permanently as can be accomplished by surgical measures. In the so-called advanced or unfavorable cases, surgery has nothing to offer, whereas radium and roentgen therapy alone, or in combination, not only relieve the patient's symptoms but establish a cure in a rather large percentage of cases.

Cancer of the corpus uteri in general is a postmenopausal disease, and is much more amenable to surgical cure than is cancer of the cervix.

In the patients not surgically operable, adequate irradiation methods will establish a cure in about 40 per cent of such cases. This is encouraging when one considers that the patient had cancer, was probably over fifty years of age and was a poor risk at the start.

In those patients whose symptom is uterine bleeding after the menopause, I would like to suggest, indeed to recommend, a more widespread use of the so-called endometrial biopsy procedure or the suction curette as an integral part of the patient's first examination by the gynecologist. Such an office investigation is feasible in most cases, and if the pathologist's report on the specimen obtained indicates cancer one can, without hospitalization for diagnostic curettage, plan and proceed promptly with treatment for the cancer.

Personally, I have been very much impressed through the years by the frequent association of fibromyomatous uterine tumors with cancer of the uterine body. About 40 per cent of our surgically treated cancers of the corpus have had coincident fibromyomata. I believe this is more than coincidence. By this I do not imply cause and effect, or that the fibromyomata are causative factors in regard to the endometrial cancer. The presence of the fibromyomata in the uterus indicates to me that this particular patient's uterus has tumor growing tendencies and therefore requires close watching.

So impressed have I been by the occurrence of cancer of the corpus after the menopause in association with the larger fibromyomata, 5 cm. or over in size, that I am inclined to advise hysterectomy as a prophylactic measure in such patients. If this is not done, the patient should be instructed to report for examination every six months. Irradiation has little value in reducing the size of fibromyomata after the menopause and should not be used.

Ovarian cancer is the gynecologist's bête noir. It occurs at all ages but especially after puberty. In fact, the most malignant histological types occur in the years immediately following puberty.

This type, common to young women, is extremely amenable to roentgen therapy, and seemingly miraculous cures have resulted in some instances. In general, however, our experience indicates that the primary cancerous ovarian growth or tumor is not radiosensitive and will not disappear after roentgen or radium irradiation.

On the other hand, secondary intraperitoneal ovarian cancer implants, as well as residual disease after incomplete operation, frequently regress or completely disappear under irradiation.

Ovarian tumors as such you can see present puzzling diagnostic problems. It seems to me the important fact to bear in mind is that about 25 per cent of all ovarian tumors are malignant; therefore, a diagnosis of ovarian tumor should mean immediate operation, if the case is operable. One should not delay, for unfortunately there are no symptoms that will permit one to make with accuracy an early diagnosis of ovarian cancer.

The end-results in the treatment of ovarian cancer today are deplorable, whether surgery or irradiation, or a combination of both, is used.

Thus, I come to the end of my lecture and I fear I leave you where we began.

Whither are we going?

PRESENTATION OF THE JANEWAY MEDAL FOR 1942

The Janeway Lecture is usually delivered upon the afternoon of the first day of the annual meeting of the American Radium Society. The medal is presented to the lecturer at the banquet held that evening. The 1942 medal was presented to Dr. William P. Healy of New York by the chairman of the Janeway Lecture Committee, Dr. Douglas Quick, with the following remarks:

This medal is being awarded Dr. Healy for his work in cancer. We are all deeply appreciative of that work and have the utmost respect for it. However, there are other things for which we might hand other medals to Dr. Healy. His work in cancer has been supported by a marvelous background of attainment before he came to the Memorial Hospital to take over the Department of Gynecology.

His long period as Associate Gynecologist to the Roosevelt Hospital very amply fitted him for taking on a special branch of gynecology. Prior to that, in the making of a well rounded gynecologist, he had the fine training of a general surgeon. That probably explains to you why he is never at a loss when he peeks over the brim of the pelvis and sees something wrong in the adjoining territory; he is always able to take care of it.

Many of you may not know that Dr. Healy was at one time Dean of the Faculty of Medicine and Professor of Gynecology to the Fordham University Medical School.

In addition to being, for these many years past, the Gynecological Surgeon of the Memorial Hospital, he is also the Associate Professor of Gynecology to Cornell University Medical School—for all of which we might award him other medals; for his teaching, particularly.

Then, too, his contributions to organized medicine in general have been by no means small. He has been President of the New York County Medical Society and he has done very extensive and real yeoman work in organized medicine in our Community and in our State.

It would be imposing too much upon the good nature of this dinner assembly if I were to attempt an enumeration of the various fine traits in the personal and social side of our Janeway Lecturer and honored guest of this evening. I would probably lose all sense of time.

These are only a few of the little things for which I might offer these extra medals, but I think that a gentleman who has done all of the things that he has and has done them so well must have some special reason back of it all. I think we have to come 'round to the fact that it's just a red-headed Irishman born on the 17th of March, and being born on the 17th of March naturally Patrick had to go into his label.

We have the privilege of honoring not only a wonderful Irishman but a fine professional gentleman and a very loyal friend.

Pat Healy, it gives me very great pleasure to present to you, on behalf of the American Radium Society, the Henry Harrington Janeway Medal.

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THE DUST HAZARD IN TREMOLITE TALC MINING, INCLUDING ROENTGENOLOGICAL FINDINGS IN TALC WORKERS

By WILLIAM SIEGAL, ADELAIDE ROSS SMITH, *and* LEONARD GREENBURG

From the Division of Tuberculosis, New York State Department of Health, and the Division of Industrial Hygiene, New York State Department of Labor

FROM time to time the attention of the Division of Industrial Hygiene has been drawn, through compensation claims, to incapacitating fibrosis in talc workers. Since silicate dusts, of which talc is one, have been considered relatively innocuous in the opinion of most authorities (the single exception being asbestos), the occurrence of these cases has naturally raised several questions—the obvious question as to whether this incapacity has resulted from talc exposure alone, and the second more interesting question as to whether industrial hygienists, with few exceptions, have erred in considering asbestos to be the only injurious silicate dust.

In an attempt to answer these questions, the study here reported was undertaken. It consisted of an investigation of the talc industry and an examination of talc miners and mill workers in northern New York State (St. Lawrence County) made, in 1940–1941, as a joint enterprise of the Division of Industrial Hygiene of the State Department of Labor and the Division of Tuberculosis of the State Department of Health.

NATURE OF TALC

Talc is a hydrous magnesium silicate with the formula $H_2Mg_3(SiO_3)_4$ composed, according to Ladoo[13] of about 63 per cent SiO_2, 32 per cent MgO, and 5 per cent H_2O. It is usually a secondary mineral resulting from the alteration of other magnesium silicates or carbonates. While its own silica is present in the combined form, most talcs mined commercially contain varying amounts of such impurities as quartz, calcite, dolomite, iron oxide, etc.

Talc has a characteristic soapy feeling and a pearly lustre. It may be pure white, silvery white, gray or green and, when impure, yellow, brown or reddish. The most common commercial variety is a massive, foliated, or granular type, but it may also occur in a micaceous, or in a fibrous form.

Soapstone is a closely related substance, being essentially an impure talc, and when pulverized it may be used for the same purposes. Tremolite, which is a calcium magnesium silicate, changes over to talc. It may be mined with it and subsequently ground and sold as talc.

GEOGRAPHICAL DISTRIBUTION

The United States produces about 65 per cent of the world's supply of talc, the leading states in its production being Vermont, New York, California, North Carolina and Georgia.

THE INDUSTRIAL USES OF TALC

According to the Minerals Year Book (1938) of the United States Bureau of Mines, the use of talc and soapstone is steadily increasing. Ladoo[13] states that at least 60 different uses for talc have been noted, though most of them are of minor importance. Its value depends chiefly on its usefulness as a filler, inert extender, dusting powder and absorbent. In 1921, according to Ladoo, the marketed, ground talc production in this country was industrially distributed as follows: paper 38 per cent, paint 23 per cent, prepared roofing 18 per cent, rubber 9.5 per cent, textiles 4 per cent, toilet powder 2.5 per cent, other uses 5 per cent.

The other uses for which ground talc is adapted are: as a filler in soap; in foundry facings; in wire-insulating compounds; in dry lubricants; as a filler in cotton textiles; in the dressing and manufacture of leather; as a cleaning and polishing agent for rice, peas, coffee beans, peanuts, etc.; in making colored crayons; as a filler in windowshade cloth; as a dusting agent in making candy, chewing gum, etc.; and as an ingredient of concrete, plastics and insecticides.

Since 1921 there has been a marked increase in its use in the ceramic industry. Fourteen thousand more tons of talc and related materials were sold in 1937 than in 1936 and about 10,000 tons of this increased amount went to the ceramic industry where talc is chiefly used as constituent of glazed wall tile.

REVIEW OF LITERATURE ON THE EFFECTS OF TALC DUST

Experimental Studies. During the last ten years a certain amount of experimental work with talc dust has been reported, but on reviewing this literature most of the inhalation experiments are found to have been of insufficient duration to be helpful in regard to the probable effect of long continued industrial exposure.

In 1931, Haynes[10] included talc in a series of dusts studied for their reactions on guinea pigs. Twelve pigs were dusted two hours daily, except Sunday, for a fortnight. The author saw no sign of pulmonary damage, but found that bronchial and lymphatic removal occurred unusually briskly. He concludes that the substances dissolved from talc are of a low degree of toxicity but sufficiently obnoxious to neighboring tissues to cause the removal of cells containing them.

Stüber,[22] in 1934, studying the cellular response of lymph nodes to various dust suspensions introduced into the lymphatics, found that talc caused no apparent cellular proliferation within the lymph nodes after five days. After 108 days the nodes were still normal and showed no increase in connective tissue.

Fossel,[6] in 1935, reported experiments in which guinea pigs were exposed to the inhalation of talc for one hour daily over a period of eight weeks. No significant tissue changes were seen.

Bethune,[2] in 1935, was able to produce pleural adhesions in cats and dogs by blowing commercial talc into the pleural cavity. Miller and Sayers, quoted below, found that adhesions were produced by injecting various dusts into the peritoneal cavity, but that such adhesions were not related to the subsequent behavior of the dust.

Fienberg,[5] in 1937, having observed granulomas from the surgical use of talc, experimented with the injection of this substance in mice and obtained subcutaneous granulomas in these animals.

Miller and Sayers,[17] in 1936, reported studies in which talc was included among the dusts whose intraperitoneal reaction in guinea pigs was studied. They found that it produced an "inert reaction." That is to say, the injected dust was not absorbed; neither did it initiate a cellular proliferation. In interpreting the significance of "inert reactions" the authors conclude that such dusts should be considered as potentially harmful.

Gardner,[7] summarizing experimental work on silicate dusts at the Saranac Laboratory said, at the Fourth Saranac Laboratory Symposium on Silicosis (1939), "a few silicates like true talc . . . and some of the clay minerals have provoked chronic inflammation (of the lungs) but this reaction has tended to retrogress after several months. No progression to a stage of true fibrosis has been observed within periods of one to two years and there is no indication that the progression will occur."

Policard,[20] in 1939, reported an experiment in which he dusted white rats with foliated, industrial talc three hours a day for twelve days. The intensity of the exposure was high. He found that the dust was irritating to the upper respiratory tract and produced a marked dyspnea. In the lungs of animals sacrificed two and six days after inhalation began, he found dilatation of bronchi, acute emphysema, and exudative alveolitis. Many animals died spontaneously with pulmonary congestion and foci of bronchopneumonia. The short duration of the experiments did not permit any conclusion concerning the possibility of pulmonary fibrosis.

McCormick and Ramsey,[15] in 1941, reported postoperative, peritoneal granulomatous inflammation caused by talc in 2 cases.

Schulz and Williams,[21] in 1942, injected intra-

peritoneally in guinea pigs a series of seven commercial talcs with different silicate-carbonate ratios. Animals were sacrificed at intervals ranging from ten days to fifteen months. In all cases, the pathological histology showed the holding of talc particles in a local area by phagocytic cells of the macrophage and giant cell type. Progressive fibrosis was not found. The fibrosis which occurred was only enough to hold and limit the space for storing the foreign material. The greatest amount of fibrous tissue developed in the presence of the two talcs which contained the least carbonate and the most talc and tremolite respectively.

Clinical Reports. Talc fibrosis as an occupational disease has received attention in this country only within the past ten years, and until the studies of Dreessen and DallaValle, discussed later, extremely few talc workers had been studied anywhere.*

Policard[20] says that it was in 1896 that the question of the action of industrial talc dust on the human lung was first considered. At that time a pathologist of Nuremberg, Thorel, published the results of the pathological examination of the lung of a tuberculous woman patient of forty-four years, who had worked for many years in soapstone dust. According to Policard, Thorel demonstrated the presence of cells containing soapstone dust in the cavity and walls of certain alveoli and the existence of formations, more or less nodular, resulting from the accumulation of cells filled with talc. Other nodular formations of a tuberculous nature were present, and Thorel pointed out a combination of tuberculous and pneumoconiotic lesions.

In 1915, according to Policard,[20] Hayburst stated that work in talc dust favored and exaggerated tuberculosis, but the basis for this opinion is not known.

Zanelli, in 1931, quoted by Teleky,[23] came to the conclusion that talc dust, though belonging to the family of silicates, ought to be considered dangerous and likely to produce typical pneumoconiotic lesions.

Merewether[1] in 1933, reported the cases of 11 rubber tire workers, exposed from ten to thirty-two years to French chalk, a fine granular variety of talc dust, who showed diffuse interstitial fibrosis by roentgen examination without clinical evidence of anything more than a peribronchial increase in fibrous tissue. Thirteen additional workers, with exposures of from four and one-half months to forty-eight years, were examined and reported upon the following year[1] confirming the original findings.

In 1933 a report was made by Dreessen[3] of examinations of a number of workers in silicate dusts, including 57 men exposed to tremolite, a hydrous calcium magnesium silicate containing no free silica.

The findings in this group were as follows: more fibrosis than usual 67 per cent, first stage pneumoconiosis 26 per cent, second stage pneumoconiosis 2 per cent, normal lungs 5 per cent.

Dreessen described the first stage pneumoconiosis as similar to that produced by cement dust; "softer" than that resulting from silica dust, a "diffuse, fine, generalized fibrosis . . . chiefly confined to the lower two-thirds of the lung fields."

In 1935 the same author, together with DallaValle,[4] reported on the effect of exposure to dust in two Georgia talc mills and mines. The dust involved was, again, a calcium magnesium silicate containing no free silica. It was present in excessive amounts, over one and one-half billion particles per cubic foot in some operations, the particle size averaging less than 1 micron. Sixty-six workers were examined. Among these, 22 (33 per cent) showed pneumoconiosis, 8 in stages two or three. The conclusion was reached that exposure to talc dust was either "too severe" in the Georgia study, or that this talc was a more dangerous dust than that previously studied. No particular relationship between talc exposure and tuberculosis was demonstrated.

Middleton,[16] in 1936, referred to an unpublished case of Cunningham's in which pneumoconiosis was found in a talc grinder who had been employed for nine years. He also mentioned an autopsy by Sand in 1910 on a woman exposed to talc dust in which "not much reaction" was found.

In 1938, Nuck and Szczepanski[19] reviewed the literature on talc fibrosis and added several cases of their own. They concluded that this type of pneumoconiosis resembled asbestosis more than silicosis.

At the International Conference on Silicosis

* Since this report was written, Porro, F. W., Patton, J. R. and Hobbs, A. A., Jr. (Pneumoconiosis in the talc industry. Am. J. Roentgenol. & Rad. Therapy, April, 1942, *47*, 507–524) have described pneumoconiosis in 15 tremolite talc workers with a fatal termination in five.

at Geneva in 1938,[12] Riddell reported the results of the examination of 37 workers engaged in grinding talc ore. Thirteen showed fibrosis resembling silicosis.

Gardner on the same occasion[12] said that of 300 films of talc workers which he had examined about 50 showed some evidence of pulmonary reaction which in 17 suggested nodulation.

From a survey of the literature it appears that while experimental studies have hitherto been inconclusive, clinical studies have tended to indicate that talc dust is capable of producing injurious pulmonary changes.

COMPENSATION CLAIMS FOR DISABILITY DUE TO TALC DUST IN NEW YORK STATE

The cases which originally drew the attention of the Division of Industrial Hygiene to disability resulting from exposure to talc dust are summarized below. Six such cases have occurred during the past few years. One originated in the manufacture of talcum powder; one in the shoe industry, and 4 of them in talc mining and milling. In one case (Case v) there had been significant previous exposure to dust probably containing free silica. Five of the 6 cases were fatal. In 5 cases, summaries are available as follows:

CASE I. Aged sixty-three. The claimant had worked for twelve years operating a talcum powder mixing machine not provided with exhaust ventilation for dust control. The talc used was found by the Division of Industrial Hygiene to contain less than 0.5 per cent of free silica. The dust concentrations at this work ranged from 13.9 to 34.8 million particles per cubic foot.

For three or four years before quitting the job, the claimant had complained of cough with expectoration. *Examination of the lungs* showed moist râles at the bases. The vital capacity was 2,500 (normal estimated as 4,000).

Roentgen examination of the lungs showed an increase of bronchial markings in the lower and middle fields with areas of increased density resembling lipiodol or calcific deposits in both midlung fields.

A *diagnosis* was made in hospital of emphysema and chronic bronchitis with acute exacerbation.

CASE II. Aged forty-four. For twenty-two years the claimant had worked as a "bed laster" in a shoe factory. White shoes were manufactured during about five months of the year and at these times he used talc freely, dusting it on the shoes to prevent soiling of the white leather. The powder used was analyzed by the Division of Industrial Hygiene and found to contain no free silica.

For seven years before quitting work he complained of cough, dyspnea and increasing weakness. His condition finally necessitated hospital treatment.

Physical examination showed the presence of dyspnea, cyanosis and clubbing of the fingers. Examination of the lungs revealed dullness on both sides with diminished fremitus and breath sounds.

Roentgen examination of the chest showed marked, confluent, hazy mottling with nodular densities uniformly distributed. The right ventricle was hypertrophied (cor pulmonale).

The *diagnosis* was chronic pulmonary fibrosis and emphysema. The case terminated fatally nine months after admission to the hospital.

CASE III. Aged forty-nine. The claimant had worked as a talc miner for fifteen years with eight months' exposure in other mines ten years previous to his talc exposure. His illness began five years before death with shortness of breath and a productive cough. He quit work two years after the onset of symptoms because of increasing weakness, and was admitted to a sanatorium.

Physical examination showed an emaciated individual who looked chronically ill. The vital capacity was 1,800 (normal estimated as 3,000). The lungs showed dullness over the middle thirds, râles above second rib anteriorly, and posteriorly throughout. Five specimens of sputum were negative for the tubercle bacillus. The temperature was normal.

Roentgen examination showed extensive, bilateral fibrosis with infection, probably tuberculous, and this was the diagnosis.

CASE IV. Aged thirty-seven. For twenty-one years the claimant had worked in talc mines as mucker, driller and foreman. For two years before quitting work he had noticed cough, shortness of breath and pain in chest. He was easily fatigued. These symptoms caused him to enter a hospital for treatment.

Physical examination revealed no lung abnormalties but showed cardiac hypertrophy, hypertension and evidence of nephrosis.

Roentgen examination of the chest showed fine nodulation through both lung fields below the fifth posterior rib, more marked in the central lung field, an increase in hilum shadows and cardiac hypertrophy.

The clinical diagnosis was early silicosis with probable infection, hypertensive disease and severe nephrosis.

The case terminated fatally.

Case v. Aged fifty-two. The claimant had worked in talc mines for seventeen years with a previous exposure of ten years in zinc and iron mines. Illness began six years before death with cough and dyspnea. Following the initial symptoms he developed pain in chest and hemoptysis and sought hospital treatment.

Physical examination showed an emaciated individual, appearing chronically ill. The fingers were slightly clubbed. The chest expansion was limited. Examination of the lungs showed dullness on the right below the seventh spine with râles and diminished breath sounds. The sputum was positive.

Roentgen examination showed a fine miliary type of increased density on the left, a mass of increased density in the right middle lung field with evidence of excavation, and heavy fibrosis at the right base.

The clinical diagnosis was probable silicosis, complicated by tuberculosis.

Death occurred twenty-one months after admission to the hospital.

Report of a Study of Talc Miners and Millers in St. Lawrence County, New York

Scope of Study. In the course of this investigation studies of operations and dust concentrations were made by engineers of the Division of Industrial Hygiene in three talc mines and five talc mills. Two hundred and twenty-one men from seven plants received an initial roentgen examination. In the case of 28 of these individuals, who showed positive lung findings, a follow-up examination was made at the end of ten months which included a second roentgenogram, a medical history and physical examination of the chest, and a detailed occupational history.

The roentgen examinations were made with a 200 milliampere machine mounted on a truck belonging to the Division of Industrial Hygiene.[11] Patterson high speed screens were used, and exposures were made at a 60 inch distance and with an exposure time of one-tenth of a second.

Type of Talc Involved. The type of talc produced in St. Lawrence County is of the fibrous variety known as asbestine. It is noted for its clear whiteness and is used chiefly as an ingredient in the manufacture of paint and tile. With it is found tremolite —calcium magnesium silicate ($CaMg_3(SiO_3)_4$)—a similar appearing mineral occurring in a fibrous or asbestiform state which in the course of time changes over to talc. Gardner[8] reports that anthophyllite, another fibrous silicate, is also present in the talc deposits of the St. Lawrence County region.

Analysis of representative samples of talc from two of the mines in the region, submitted by one of the mining companies, shows the following composition:

Analysis	*Sample A*	*Sample B*
Total silica*	68.24	57.50
Calcium oxide	2.72	5.24
Aluminum oxide	—	.27
Iron oxide	—	.17
Manganese oxide	—	.16
Carbon dioxide	—	.38
Magnesium oxide	24.51	30.20
Calcium carbonate	0.23	—
Sulfur trioxide	trace	—
Ignition loss	3.65	5.13
	99.35	99.05

Free silica content. The free silica content of commercial talc as found in industrial use is very low. Schulz and Williams[21] report that of 51 samples analyzed quartz was not found in 25; traces of quartz only were present in 25; while one sample showed a quartz concentration of 3 per cent. The free silica content of the talc in the mills and mines included in this study was likewise found to be low. Six samples from two talc mines, taken and analyzed by chemists of the Division of Industrial Hygiene, showed 1 per cent or less of free silica. Two of these samples were taken from long standing accumulations of waste rock; two were

* Includes both free and combined silica.

FIG. 1. Tremolite talc. Note bundle-like arrangement of fibers. (Magnification 2,500×.1 inch = 10 microns.)

from recent three- and four-day-run waste accumulations; and two were from collections of rock destined for the mills. Six samples of ground talc from several mills were also analyzed and in each case the silica content was found to be less than 1 per cent. Dreessen[3] also reported little or no free silica in the composition of the talc in this region.

Gardner,[8] on the other hand, found amounts of quartz ranging from 12 to 20 per cent in mineral samples from two mines in this area. It is difficult to explain the marked difference between Gardner's findings and those of Dreessen[3] and ourselves, except upon the supposition that Gardner's samples included some of the quartz-bearing stratum overlying the talc deposit proper. That such high percentages are not representative, however, is shown by the

FIG. 2. Tremolite talc. Note straight needle-like fibers. (Magnification 2,500×.)

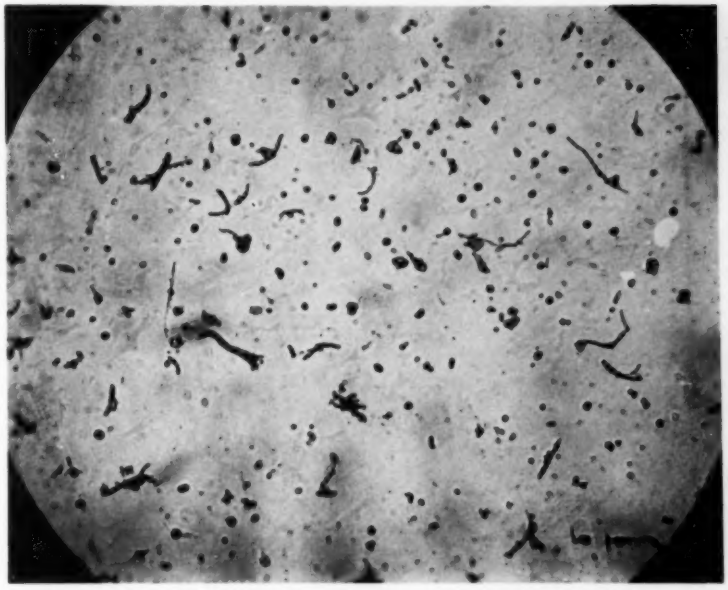

Fig. 3. Asbestos. Note curving tendril-like fibers. (Magnification 2,500×.)

fact that material from the mills where all rock is mixed and crushed showed low quartz percentages both in Gardner's studies and our own.

Microscopic appearance. Photomicrographs of talc dust from St. Lawrence County show that it tends to occur in oblong or squarish particles made up of parallel fibers (Fig. 1) which splinter off into sharp spicules (Fig. 2). Its microscopic appearance differs from that of asbestos (Fig. 3) in that asbestos fibers tend to be curved and tendril-like in form, whereas those of talc appear straighter and needle-like in structure. Tremolite talc fibers are also much shorter than those of asbestos. In this study their maximum length was approximately 15 microns. Asbestos fibers, on the other hand, may attain a macroscopic length. In interesting contrast to both tremolite talc and asbestos are the flake-like particles of mica dust (Fig. 4), another

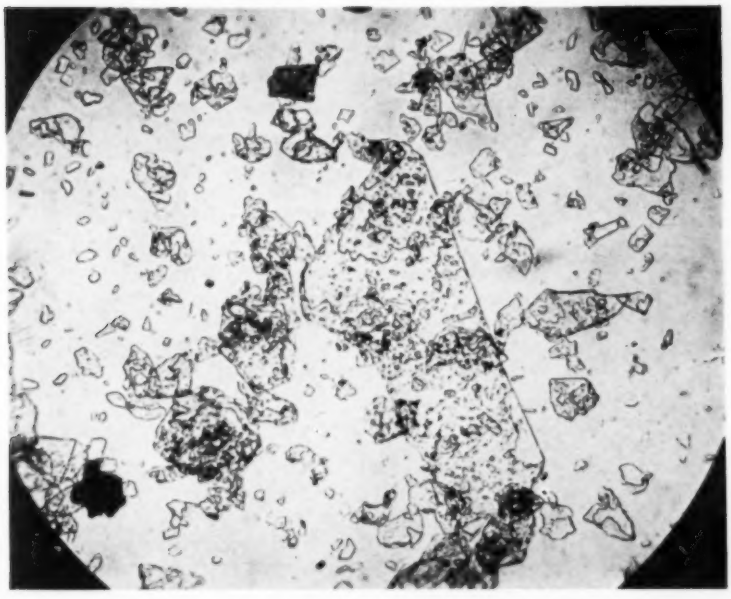

Fig. 4. Mica. Typical mica particles, showing the very thin plate-like structure. (Magnification 2,500×.)

magnesium silicate, and the granular particles of granite dust (Fig. 5), a combination essentially of quartz and feldspar.

Description of the Industry

Talc Mining

Mining operations. Talc ore is obtained by underground mining. Inclined shafts are used with headings to various depths down to about 1,100 feet. The talc occurs in compact, homogeneous seams, so that contact with hard rock is limited to that incurred on entering a seam. Once a seam is entered there is no exposure to anything but talc until it becomes necessary to enter another seam. Since seams may be worked for years, the amount of drilling in hard rock is very small compared with the amount of drilling in talc.

The headings are mined by drift drilling, blasting, and hand or machine mucking. Raising and stoping are resorted to, to obtain the ore from pockets. All drilling is done dry since every precaution must be taken to avoid wet ore which cannot be milled and is wasted. Drilling crews of one or two men are used, the drillers doing their own blasting. The ore is then mucked as it is required by the mills. It is loaded into muck cars and pushed along the haulageways to the shaft where it is dumped into a skip, hoisted to the surface, and dumped into railroad cars or trucks for shipment to the mills. Each mine employs fifteen to seventeen men underground.

Dust exposure in talc mining operations. The problem of the best method of control of the dust in talc mines is one which is receiving the attention of the Division of Industrial Hygiene at the present time. Very little dust control was found in the three mines studied. Some attempts had been made to remove the dust during drift drilling by means of small, home-made, portable units, but relatively few of these were in actual use during drilling operations. The drillers wore respirators.

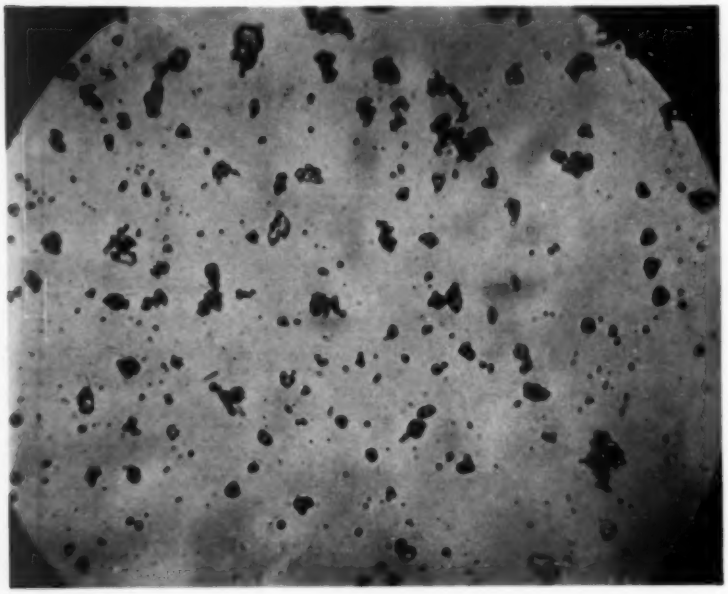

FIG. 5. Granite. Shows lack of form usually found in silicate and silica particles. (Magnification 2,500×.)

Twenty-two dust samples were taken with a midget impinger at various operations and situations. These were counted within ten hours of the time of sampling by means of the low power, light field technique, and gave the results shown in Table 1.

The dust counts where no exhaust device was used gave average dust concentrations as follows: for drilling 1,350, for stoping 1,290, for mucking 35, and in the general air, 17 million particles per cubic foot.

Talc Milling

Milling operations. The milling processes in all five mills were found to be essentially alike. The ore is shipped to the mills in railroad cars or trucks and is dumped into chutes leading to a jaw crusher. From the jaw crusher the talc, in most mills, passes through disc or roll crushers, or both, before entering rotary or trommel screens. After passing the screens, the talc is stored in garners before the final milling operation which takes place in pebble mills. The final separation of the finely ground talc is accomplished with air separators, from which the material passes to garners which feed bagging machines.

The bagging machines utilize open top bags, or sacks, which fit loosely onto the discharge spout of the machines. Hand scoops are used to add or remove talc from the bags to obtain accurate weight. The greater percentage of material is bagged in

TABLE I

DUST CONCENTRATIONS IN TALC MINES

Operation	Mine	Dust Count (million particles per cubic foot)	Remarks
Drilling	A	200	"Upstream" of drill. Rate 2′ per minute
		300	"Downstream" of drill
		75	3′ "upstream." Using exhaust
		110	Same as above. Breathing level of helper
		600	Exhaust off
		2700	Exhaust off. Breathing level of helper "downstream"
		5000	Exhaust of dust collector
		1500	Same as above; 3 minutes after drilling stopped
		150	General air stream
	B	65	"Upstream" air movement 50′ per minute
		265	Same as above. Air turbulent
	C	90	Dead end drift
		300	Just off main airway
		16	Main airway
		100	Breathing level driller, top of open stope
Stoping	A	4000	Dead end stope. No air movement
	B	760	Top of dead end raise
Mucking	A	40	Bottom of stope, drilling at top
		50	Same as above
		6	Top of pile, mucking only operation
	B	35	"Downstream" of mucker
		24	Same as above

TABLE II

DUST CONCENTRATIONS IN TALC MILLS

Operation	Mill	Dust Counts (million particles per cubic foot)	Average Dust Concentration (million particles per cubic foot)
Crushing-jaw crusher	1	20	
	2	41.5	
	3	76.5	46
Crushing-disc or roller crushing	1	22	
	2	79	50
Pebble milling	1	32	
		46	
	2	106	61
Bagging—paper	1	141	
	2	190	
	4	160	163
Bagging—burlap	1	120	
	3	73.5	
	5	87.5	93
General air cylinder room	1	48	
	3	85	
	4	78	
	5	77	72
Separator room	4	58	
	5	67.5	62
Manual handling	1	215	

50 lb. paper bags, while some is shipped in larger burlap bags. The operators of the bagging machines stack the filled bags on hand trucks and wheel the loaded trucks into railroad cars or automobile trucks for shipment, or into the warehouse for storage.

Dust exposure in talc milling operations. Dust control in the various mills is confined chiefly to the bagging machines and pebble mills. Some control is also used in several mills at the crushers and material transfer points. Dust samples were taken throughout the mills using the technique already described. The samples were taken at the breathing level of the workmen in locations where men are usually stationed.

Table II shows the concentrations found at various points throughout the mills. Manual handling of the talc produces concentrations in excess of those found at other operations but, fortunately, there is little manual handling during normal procedure.

The dustiest operation, other than manual handling, is that of paper bagging where the average dust concentration for three mills was found to be 163 million particles per cubic foot.

TABLE III

FIBROSIS IN TALC WORKERS, BY LENGTH OF EXPOSURE

Years Exposed	All Workers Examined	Cases of Fibrosis		
		Number	Total Fibrosis Cases per cent	Exposure Group per cent
5	82	—	—	—
5–9	32	—	—	—
10–14	47	8	25.0	17.0
15–19	33	13	40.6	39.4
20–24	10	2	6.3	20.0
25–29	9	3	9.4	33.3
30–39	6	5	15.6	83.3
40–49	1	—	—	—
50–59	1	1	3.1	100.0
Totals	221	32	100.0	14.5

Roentgen Findings

Fibrosis

Incidence. In recording pulmonary fibrosis among talc workers, those with slight or even moderate degrees of fibrosis were disregarded, and only those cases included in which a marked degree of this condition was present.

Upon the initial roentgen survey in 1940 fibrosis was found in 32 of the 221 men examined, giving a rate of 14.5 per cent. The distribution of these cases according to length of exposure is shown in Table III.

It will be seen that no cases occurred in workers with less than ten years' exposure. The 32 cases of fibrosis were all found among the 107 men who had worked in talc for ten years or longer, giving an incidence rate for this group with ten years or more of employment of 29.9 per cent. Of the 8 men who had worked thirty or more years in talc, 6 showed fibrosis (74 per cent).

To make clear the fact that talc is a fibrosis-producing dust the distribution of cases of fibrosis, according to age, in talc workers and in a group of carpet factory workers previously examined by the authors, is shown in Table IV.

Fibrosis was present in only 2.5 per cent of all carpet workers, and in 4.9 per cent

TABLE IV

FIBROSIS IN TALC AND CARPET WORKERS, BY AGE

Age	Talc Workers			Carpet Workers		
	Number examined	With fibrosis		Number examined	With fibrosis	
		Number	Per cent		Number	Per cent
Less than 20	4	—	—	6	—	—
20–29	71	1	1.4	57	—	—
30–39	72	7	9.7	61	1	1.6
40–49	41	7	17.0	57	1	1.7
50–59	17	9	52.9	49	4	8.1
60–69	13	6	46.1	33	—	—
70–79	3	2	66.6	3	—	—
Totals	221	32	14.5	266	6	2.5

of those fifty years of age and older; while it was present in 51.5 per cent of talc workers in this age group.

Ten months after the original roentgen study, a second visit was made to the same plants for follow-up examinations of selected cases. At this time occupational and medical histories were taken and chest examinations were made. From the occupational histories it was possible to eliminate those men who had previously been exposed to other types of siliceous dust. In this way a group of 18 cases showing marked fibrosis was defined in men who had not worked in any other dusty industry and whose only significant dust exposure, therefore, had been to talc.

Signs and symptoms. Fifteen of the men showing fibrosis worked in the talc mills; 3 were miners. The proportion of mill workers to miners in the entire group, however, was approximately 2.3 to 1, showing that fibrosis was relatively more prevalent among millers than miners. With one exception, the men with fibrosis were all forty years of age or older and had been exposed to talc dust, as noted above, for at least ten years.

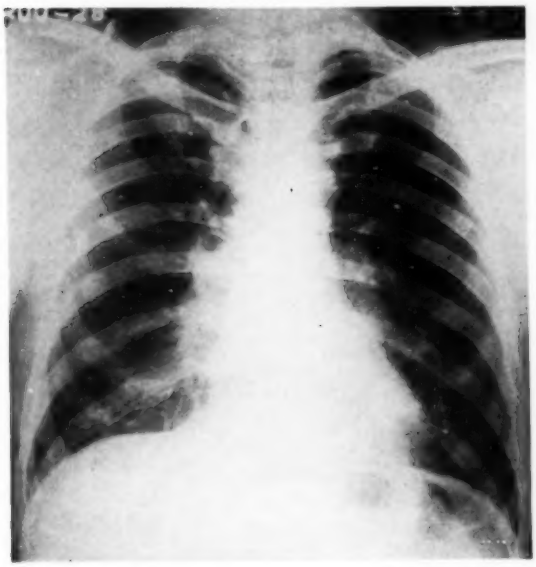

Fig. 6. Case 200-28. Aged forty-six. Began working at age of fifteen. Woolen mill six years; talc mill worker twenty-five years. Complains of cough, shortness of breath, pain in chest, fatigue. *Physical examination:* Chest expansion 1¾ inch, respiration 28, breath sounds diminished. Clubbing of fingers. *Roentgen examination:* Shows a very fine, granular fibrosis on a diffusely hazy background. The hilar nodes are thickened.

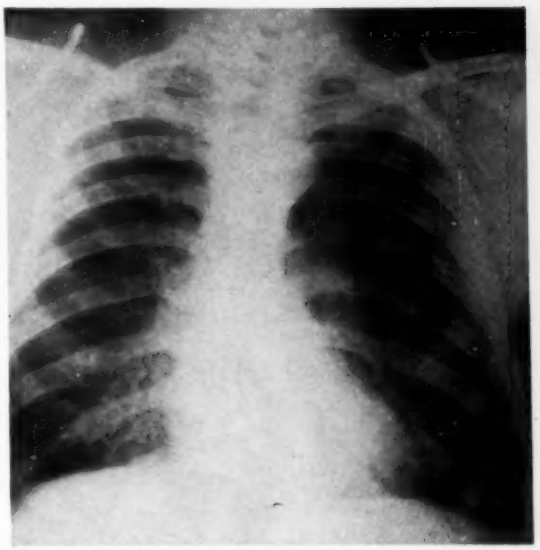

Fig. 7. Case 198-3. Aged fifty-four. Began work at age of fifteen. Farmer sixteen years; telephone linesman seven years; talc mining sixteen years. Complains of productive cough and dyspnea. *Physical examination:* Chest expansion 1 inch. Nails curved. *Roentgen examination:* Shows enlargement of the hilar nodes, and exaggerated linear markings at the right base. There is also a fine, generalized, diffuse fibrosis having a granular appearance.

Thirteen of the 18 had one or more symptoms referable to the lungs. Ten complained of dyspnea; 7 of chronic cough and 3 of pain in the chest. In addition, 5 complained of excessive fatigue.

On physical examination, all 18 showed limited chest expansion. Thirteen showed abnormal lung signs and 13 showed curving of the nails or clubbed fingers. In one case cardiac hypertrophy was observed, and in one auricular fibrillation.

The general appearance of the group struck the examiners as being distinctly different from the appearance of the usual group of first and second stage silicotics who are still able to work. The latter usually present a robust appearance. A substantial number of individuals in such a group are

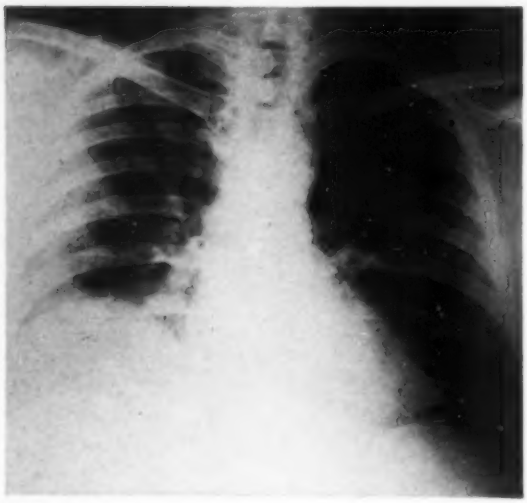

FIG. 8. Case 197-38. Aged fifty-five. Began working at age of fourteen. Talc mill laborer and foreman forty-one years. Complains of fatigue. *Physical examination:* Chest expansion 1¾ inches; clubbing of fingers. *Roentgen examination:* Shows marked elevation of right diaphragm with obliteration of the costophrenic sulcus. On the left leaf of the diaphragm is a deposit of opaque material. Both lungs show a fine, granular fibrosis.

likely to be overweight. This was not the case with the talc workers who showed fibrosis. None of them was overweight, but on the contrary they tended to present an undernourished and drawn appearance. It was the impression of the examiners, also, that dyspnea was unusually pronounced in relation to the extent of the fibrosis seen in the roentgenograms.

Roentgenographic characteristics. The type of fibrosis seen in these roentgenograms is very fine and diffuse, showing in many cases an appearance of soft haziness to which the term "ground glass," used in describing certain cases of asbestosis, can very well be applied. This is illustrated in Figures 6, 7, and 8. In a number of cases there is in addition a distinctly granular appearance (Fig. 7), and in some nodulation (Fig. 9 and 10) which might be confused with silicosis. In certain films soft conglomerations also occur (Fig. 9 and 11).

The fibrosis in these cases tends to be somewhat more marked on the right side, and in the mid-lung fields and bases as seen in Figures 7 and 9. The hilar nodes show a slight or moderate increase in density. Evidence of obliterative pleuritis and emphysema is also present in some cases. In a few instances (Fig. 7 and 11) a blurring or "shagginess" of the cardiac outline is noticeable.

Tuberculosis. In the total group of 221 talc workers there were 29 (13.1 per cent) cases of primary healed tuberculosis; 6 (2.7 per cent) cases of healed reinfection type tuberculosis and 5 (2.2 per cent) cases which were considered, on the basis of the roentgen appearances alone, to show clinically significant tuberculosis.

The incidence of healed primary and reinfection type lesions is not remarkable in any way, being similar to that found, in general, in other industrial groups. The incidence of clinically significant tubercu-

FIG. 9. Case 196-3. Aged sixty-eight. Began working at age of sixteen. Farmer twenty-three years; carpenter six months; talc mill laborer and repair man twenty-nine years. Complains of dyspnea. *Physical examination:* Chest expansion 1½ inches, respiration 24, râles both bases. *Roentgen examination:* Shows a diffuse, finely nodular fibrosis throughout both lungs. There is emphysema at the left base. There is apparent thickening of the pleura at the right base with several horizontal shadows in this region. There is also an area of increased density extending from the second to the third interspace on the right, and shadows at both apices suggesting possible reinfection tuberculosis.

losis (2.2 per cent) is slightly higher than is found in most industrial groups, the average rate found for this condition being about 1.2 per cent. Among the 5 individuals with clinically significant tuberculosis 3, between the ages of thirty and fifty, showed minimal lesions; one, forty-five years of age, showed moderately advanced lesions and one, sixty-four years of age, showed what was interpreted to be far advanced atypical tuberculosis. Among the 18 cases of fibrosis in men exposed only to talc clinically significant tuberculosis appeared to be a complicating feature in 3 cases (16.6 per cent).

Talc plaques. A most interesting finding in this group of talc workers—interesting because, to these investigators, it was new—was the presence in 14 instances (6.3 per cent of the 221 talc workers originally roentgenographed) of what appeared to be deposits of opaque material on various pleural surfaces. These deposits, or plaques, are seen on the visceral pleura, including the region of the diaphragm, and occasionally the pericardium (Fig. 8, and 13 to 17). Lateral and oblique views indicate that their location is definitely at the periphery of the lung, not involving the parenchyma (Fig. 17).

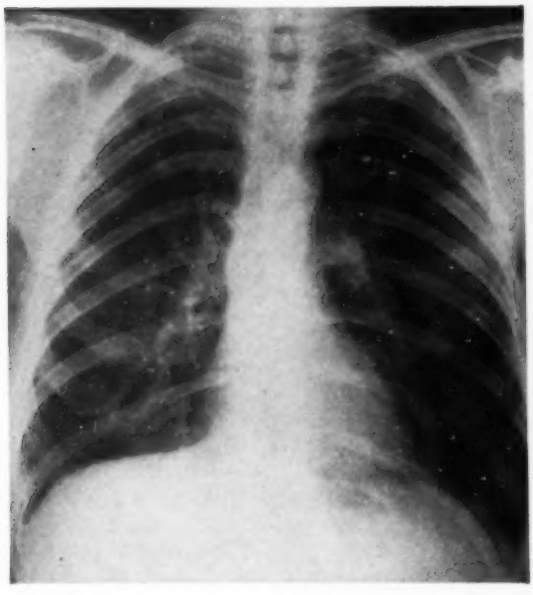

Fig. 10. Case 197-8. Aged forty-nine. Began working at age of fourteen. Talc mill laborer thirty-five years. Complains of dyspnea, pain in chest, fatigue. *Physical examination:* Chest expansion 1¾ inches. Nails curved. *Roentgen examination:* Shows diffuse finely nodular fibrosis with soft shadows suggesting bilateral, clinically significant, apical tuberculosis.

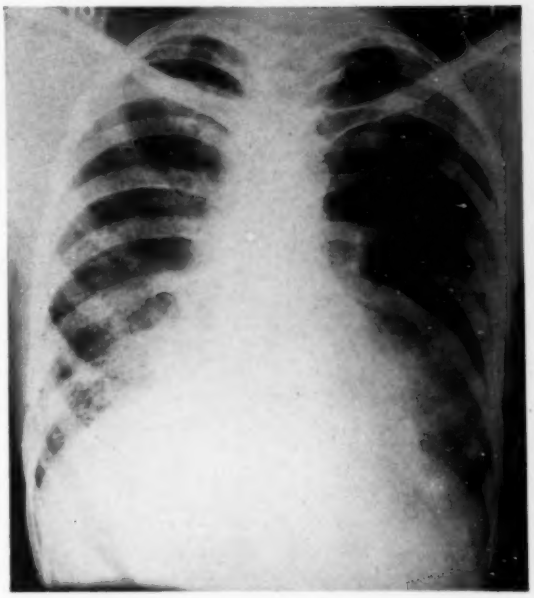

Fig. 11. Case 201-10. Aged forty-nine. Began working at age of sixteen. Farmer seven years; talc mill laborer and foreman twenty-six years. Complains of productive cough, dyspnea and fatigue. *Physical examination:* Chest flat, expansion limited, dullness at apices, otherwise hyperresonant. Râles throughout, most marked at bases. Respiration 22; pulse 116. Heart negative. Clubbing of fingers. *Roentgen examination:* Shows a fine, soft mottling over both lung fields, more pronounced at the bases. In addition, in the third left interspace near the periphery is a round homogeneous area of increased density about 2 cm. in diameter.

In size the plaques vary from a single, linear-appearing deposit of a few centimeters in length in the region of the diaphragm (Fig. 8 and 12) to massive deposits bizarre in shape, extending over a large part of the lung fields (Fig. 14, 15, 16 and 17). They are characterized not only by irregularity of shape, but by marked irregularities in degree of density also, and by the sharpness of their borders. In this series of films the development of these plaques can be traced from small, light, scarcely noticeable deposits to the extensive opacities described.

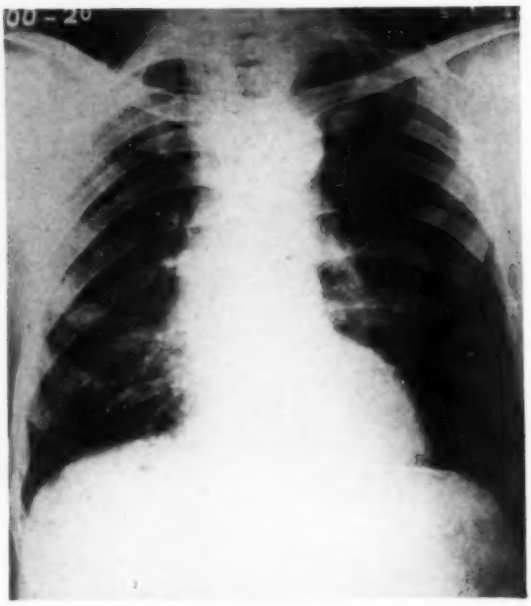

FIG. 12. Case 200-20. Aged sixty-three. Began working at age sixteen. Fireman three years; farmer eight years; talc mill laborer and repairman thirty-nine years. Complains of dyspnea and fatigue. *Physical examination:* Lungs hyperresonant. Heart slightly enlarged to left, rate irregular. Clubbing of fingers. *Roentgen examination:* Shows deposits of opaque material on the left diaphragmatic dome; marked emphysema at the left base. Both lungs show diffuse, granular fibrosis with irregular patchy shadows at right base and left midlung field.

It should be noted that roentgen appearances similar to the plaques herein described were apparently seen in Case 1 where mention is made of areas of increased density resembling lipiodol or calcific deposits in mid-lung fields. Similar appearances have also been noted in another group of workers who were exposed to talc dust in the making of material for electrical insulation.

So far as can be ascertained, these deposits bear no relation to any history of previous infection since they occur both with and without such a history. Nor are they necessarily associated with other pulmonary pathology. The underlying lung tissue may or may not show fibrosis. There is no associated enlargement of the hilar nodes in cases showing plaques without fibrosis.

An analysis of the group of 14 talc workers who showed these deposits revealed the following facts: Their ages ranged from thirty-five to seventy-seven years and their exposure in the talc industry from four to fifty-two years. Ten were mill workers; 4 were miners. Only one individual gave a history of having had pleurisy. None had had empyema. In 5 instances no lung pathology other than the plaques was noted. A marked degree of fibrosis coexisted in 7 cases. Evidence of clinically significant tuberculosis was seen in one case and of primary healed tuberculosis in another case.

No symptoms or physical signs attributable to these deposits could be identified,

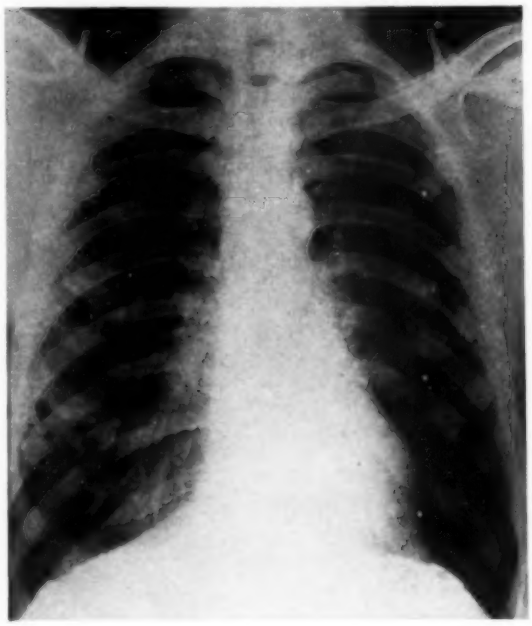

FIG. 13. Case 201-5. Aged fifty. Began working at age of fifteen. Farmer seventeen years; repairman in talc mill eighteen years. Complains of cough. *Physical examination:* Lungs show diminished breath sounds throughout, especially on right. Heart: systolic murmur at apex. Pulse 120. Clubbing of fingers. *Roentgen examination:* Shows a soft, diffuse, very finely nodular fibrosis throughout both lungs. In addition, there are irregular, sharply defined deposits of opaque material in both middle and lower lung fields. (Lateral and oblique views show that these plaques are located near the periphery.) There are similar deposits on both diaphragms and in the region of the right spinal gutter.

since in the group studied symptoms and signs only occurred in those individuals in whom there was other lung pathology. Apparently the plaques themselves and the process responsible for producing them are symptomless.

DISCUSSION

Fibrosis. The type of fibrosis found in this study was characterized, as already described, by a soft haziness and a *finely* granular or nodular appearance tending to be more marked in the mid-lung fields and bases. Dreessen[3] apparently found a condition somewhat similar to this in his study of tremolite talc workers in the same geographical area. However, the fibrosis here reported was more severe than that found by Dreessen as indicated by the conspicuous presence of clinical symptoms, such as dyspnea, pain and fatigue in these cases and also by the more frequent appearance of granulation and fine nodulation. It more closely resembled in severity the fibrosis later reported by Dreessen and Dalla-Valle[4] among Georgia talc millers and miners. Here the talc was also of the tremolite variety. Analyses also failed to show the presence of free silica. These authors reported 8 cases with symptoms of dyspnea, cough and pain, abnormal chest signs,

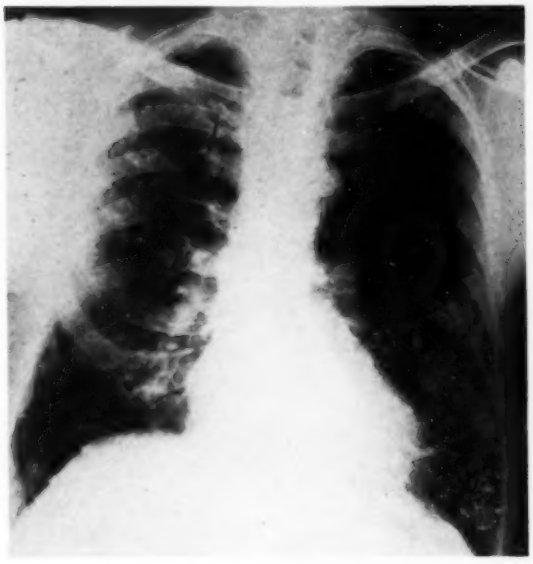

FIG. 14. Case 196-16. Aged fifty-two. Began working at age of fifteen. Farmer twelve years; worked on railroad four years; talc mill worker thirty-one years. No complaints. *Physical examination:* Chest expansion 1¾ inches, breath sounds distant. Nails Curved. *Roentgen examination:* Shows what appears to be an extensive, irregular, sharply defined deposit of opaque material in the left lung field. Stereoscopic view shows that this deposit is at the periphery, probably on the visceral pleura, and that the lung beneath is comparatively free from fibrosis. The right lung shows a fine, diffuse, granular fibrosis with shadows in the first and second interspaces suggesting healed reinfection tuberculosis.

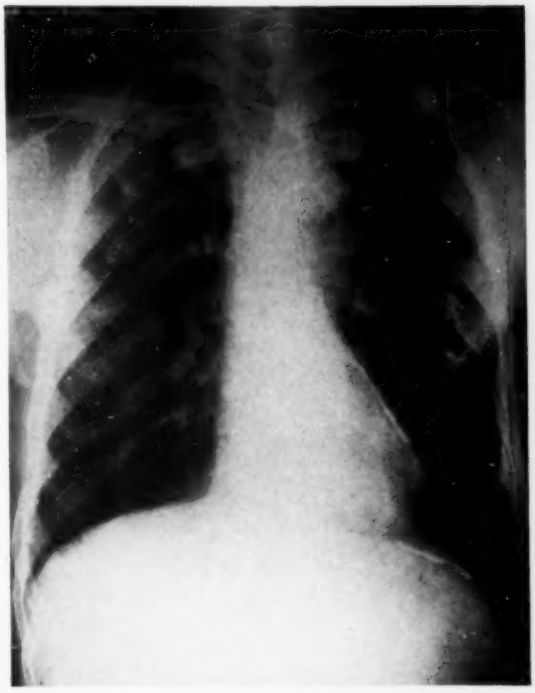

FIG. 15. Case 199-16. Aged sixty-three. Began working at age of sixteen. Talc mill laborer sixteen years; talc miner thirty-one years. Complains of productive cough, night sweats, pain in chest, loss of weight and appetite. *Physical examination:* Chest flat, expansion 1¾ inches, lungs dull both apices, diminished breath sounds, nails curved. *Roentgen examination:* Shows what appears to be deposits of opaque material on the left diaphragm and pericardium; also an extensive irregular deposit on the left pleura. Stereoscopic view indicates that the latter is on the visceral pleura. Soft shadows indicative of moderately advanced tuberculosis are present in both apices, extending to the third interspace on the right and the second on the left.

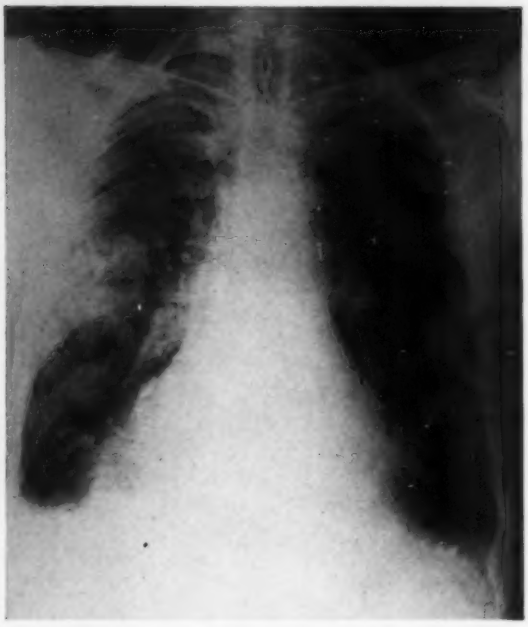

FIG. 16. Case 198-40. Aged sixty-four. Began working at age of sixteen. Paper mill five years; carpenter six years; zinc miner three years; talc miner and blacksmith twenty-one years; talc mills thirteen years. Complains of productive cough, shortness of breath, fatigue, and night sweats. *Physical examination:* Chest expansion 1¼ inches. Respiratory rate 32; pulse 112. The lungs are hyperresonant. There are bronchovesicular breath sounds with râles throughout right lung. Curved nails. *Roentgen examination:* Shows extensive areas of increased density which suggest irregularly shaped deposits of opaque material in both lung fields. This appears to be not exactly at the periphery but several millimeters inside the lung field. There is also a rather dense accumulation of opaque material on the right and left leaves of the diaphragm, along the right pericardial border and arch of the aorta. The right costophrenic sulcus is obliterated. The lung tissue, apart from the areas described, shows an increase in lung markings more marked on the right.

clubbed fingers, and a nodular or "nodular-conglomerate" type of fibrosis.

The occurrence of a type of fibrosis giving a nodular roentgen appearance as a result of exposure to tremolite talc dust is a matter of considerable interest, since nodular fibrosis is traditionally associated only with dust containing free silica. Gardner[8] attributes fibrosis in tremolite talc workers to the contaminating presence of free silica, but inasmuch as the free silica content of the twelve samples of mineral from talc mills and mines analyzed in the present study was found to be practically negligible (less than 1 per cent), it seems reasonable to suppose that the fibrosis observed in these cases is primarily the result of the inhalation of the various silicate minerals present in the dust, namely talc, tremolite and anthophyllite.

Microscopic study has shown that this dust is largely fibrous in character, and it may well be that this particular physical characteristic is responsible for the pathology of tremolite talc fibrosis. The possibility of action analogous to that which occurs in asbestosis is suggested by several facts: first, the chemical and physical similarity between the minerals in this area and those found in asbestos; second, the fact that the disability in tremolite talc fibrosis, like that in asbestosis, tends to be greater than one would expect from the severity of the lesion as seen on roentgenological examination.

FIG. 17. Same case as Figure 16. Oblique view.

Because of these similarities, the authors of this paper have taken the opportunity to compare this series of films of tremolite talc workers with those of a group of workers showing early asbestosis.* They were impressed by the resemblances in the roentgen appearances in the two groups. The talc fibrosis resembled early asbestosis in its fineness and diffuseness, its hazy "ground glass" quality and, in addition, some in the series of asbestosis films showed a mottled or nodular appearance similar to that seen in the more advanced cases of talc fibrosis.†

Whatever the exact pathology may ultimately prove to be, the study here reported clearly indicates, from a practical standpoint, that the dust encountered in the tremolite talc industry is of a definitely injurious, fibrosis-producing type which requires control in order to prevent disabling occupational disease. Moreover, although the number of cases here presented is small, suggestive evidence has been found that exposure to tremolite talc dust is associated with increased susceptibility to tuberculosis.

Talc Plaques. In regard to "talc plaques," one possibility to consider is that they represent simply aggregations of actual talc dust which has remained in the periphery of the lung unable to be disposed of in any manner. This supposition makes it difficult, however, to account for the presence of these deposits in a few cases only, rather than in the majority of those exposed.

Since "talc plaques" closely resemble, in appearance, pleural calcifications resulting from traumatic pleuritis or empyema, the thought immediately suggests itself that they are, in fact, deposits of calcium. The dust of tremolite talc contains calcium—tremolite being a calcium magnesium silicate—but so also do other dusts such as cement and marble. Why does tremolite talc dust alone produce the opaque deposits described?

Calcific deposits ordinarily presuppose previous irritation or injury. This fact suggests that tremolite talc dust, therefore, has some unique ability to irritate or injure pleural surfaces, such injury being followed by the deposition of readily available calcium. It is known, for example, that the resolution of intrapleural hemorrhage is frequently followed by calcium deposition, and one is tempted to speculate as to whether the needle-like particles present in this dust may, by tissue penetration, cause multiple, minute, capillary hemorrhages whose resolution results in the appearances described.

The location of the deposits, as seen in lateral, oblique and stereoscopic views, appears actually to be just beneath the pleural surface. This suggests that they may lie in the peripheral lymphatic network and opens up another speculative possibility. In this connection an illustrated article by Lommel[14] in *Deutsche medizinische Wochenschrift* is of great interest. Discussing the familiar "egg shell" appearance occasionally seen in hilar nodes, he reports, in certain cases of silicosis, large calcific deposits in the peripheral parts of the lung which, to judge by the illustrations, closely resemble "talc plaques." His suggested explanation is that calcium (lime) is laid down in inflamed fibrous tissue in the congested lymph spaces which form a network around the lobules of the lung.

The sharply demarcated, yet irregular, borders of the "talc plaques" do in fact suggest that the deposit of opaque material is definitely limited as by the outlines of some irregularly shaped structure such as the walls of lymphatic spaces. It is of interest in this connection that Gardner and Cummings,[9] working with asbestos, report well marked hyperplasia and dilatation of lymphoid tissue in the periphery of the lung in guinea pigs which they believe may be the result of pulmonary irritation. One may speculate as to whether tremolite talc may not produce a similar condition which is then followed by the deposition of calcium already present in the dust.

* Through the courtesy of Dr. W. J. McConnell of the Metropolitan Life Insurance Co., New York City.

† "Mottling" in asbestosis has been described by Merewether[1] and also by Gardner and Cummings.[9]

Another interesting feature of the cases showing talc plaques is that radiopaque material in these cases is not, apparently, deposited in the hilar nodes. This suggests that talc dust does not find its way to them in large amounts. If this be true, it would indicate a similarity in this respect to asbestos which, as Gardner and Cummings have shown, tends to be held in the periphery of the lungs.

Whatever the similarity in effect between asbestos and talc dust, however, one conspicuous dissimilarity is the absence of any change resembling "talc plaques" in the lungs of asbestos workers. In fact, as far as we are aware, with the single exception of the German reference[14] given above, such deposits have not heretofore been described in connection with any dust.

SUMMARY

1. A study of the tremolite talc mining and milling industry in northern New York State is reported.

2. Talc in this region is of the asbestine variety, mingled with tremolite and anthophyllite. Analyses of material from both mines and mills gave consistently a free silica content of 1 per cent or less. Microscopic studies of dust showed the presence of fine, straight, needle-like fibers.

3. Dust counts in mining ranged from 6 to 5,000 million particles per cubic foot; in milling from 20 to 215 million perticles per cubic foot.

4. In a group of 221 tremolite talc miners and millers advanced fibrosis was found in 32 men, giving an incidence of 14.5 per cent.

5. All of the cases of fibrosis occurred among those men who had worked in tremolite talc for ten years or longer (107 men), giving an incidence for this group of 29.9 per cent.

6. The fibrosis found in this study was of a fine, diffuse type with a roentgenographic appearance of granulation or nodulation on a hazy background. It tended to be disabling in character and was frequently accompanied by dyspnea, cough and fatigue.

7. There was also some evidence that this fibrosis was characterized by an increased susceptibility to tuberculosis. Clinically significant tuberculosis was diagnosed by roentgen examination in 3 of 18 cases of tremolite talc fibrosis where there had been no other dust exposure.

8. In addition to fibrosis, deposits of unidentified opaque material in the periphery of the lungs, including the region of the diaphragm and pericardium, designated as "talc plaques," were observed in 6.3 per cent of all tremolite talc workers examined. These deposits occurred independently of other lung pathology and could not be identified with any particular signs or symptoms.

CONCLUSIONS

This study identified tremolite talc as a silicate dust capable, like asbestos, of causing a disabling pneumoconiosis. It reveals distinctive pathological findings associated with exposure to tremolite talc dust which postulate a special etiology for the resulting disease. There is also evidence that tremolite talc fibrosis is associated with an increased susceptibility to tuberculosis.

In the light of these findings, exposure to tremolite talc dust must be considered to constitute a definite industrial hazard requiring control of dust by suitable engineering methods.*

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* Since this paper was written, an article on experimental production of intrapleural adhesions in animals by Hanrahan, Adams and Klopstock has appeared in the Fifty-Seventh Annual Medical Report of the Trudeau Sanatorium. In the case of one rabbit treated with iodized talc, the authors report, "The medial half of the diaphragm contained a subpleural collection of powder, 0.5 mm. in thickness, lying in situ as a semirigid plaque. . . . Mediastinal and diaphragmatic distribution suggested complete lymphatic blockage."

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VIRUS PNEUMONIA

ROENTGENOGRAPHIC CHARACTERIZATION OF RECENT VIRUS PNEUMONITIS WITH BRONCHOPNEUMONIA

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THE paucity of autopsy material available for the study of virus pneumonitis is an academic handicap, but enough of a humane blessing to allay regret; these circumstances place an emphasized burden of responsibility on bacteriologic consultants and deductive forms of clinical analysis. Not the least of the latter is, we believe, accurate roentgenographic observation and deductive correlation of findings.

The characteristic roentgenographic appearance, the characteristic distribution, and the fairly characteristic changes in evidence of development and recession—resolution—of lobar (pneumococcus) pneumonia are uniform, dependable and well known. Since this disease entity provides, such a regular syndrome of history, symptoms, physical signs, bacteriologic findings and short routine typical course, roentgenographic examinations have come to fill an order of somewhat secondary importance in lobar pneumonia. Roentgenologic consultation is important largely for the following:[18]

A. A study of correlative findings in early stages of a relatively typical syndrome.
   1. Verification of physical findings, rarely necessary in frank cases.
   2. Localization of process; more important on the right side of the chest.
   3. Record of conditions as a clinical course-record "base line".
   4. Identification or exclusion of any coexistent complication.

B. Study of special phases of early stages of not-so-typical syndrome.
   1. Identification of process, in case of vague history and physical signs.
   2. Especially in the face of symptoms and/or signs outside of the thorax: in the abdomen, meninges or central nervous system.
   3. Or identification of late phase of previously unrecognized pneumonic process resulting from mild pneumococcic pathogen.

C. Differentiation of a case at hand from a multitude of other intrathoracic diseases when the history, physical findings, or course seem unreliable.

D. Serial studies in case of complication both immediate and presistent such as empyema, delayed resolution, chronic fibrosing non-resolution, and/or subsequent bronchiectasis, acquired type.

The group designated under C above would likely include the disease entity, as we choose to call it, which forms the nucleus of interest in this presentation.

LITERATURE

As early as 1932 and 1933 French[3] and German[22] authors were describing a typical pneumonic process with atypical distribution, usually not involving even a large part of a single lobe, apparently not always accompanied by pneumococcus infection. "These cases," if they may be successfully grouped, were soon (1935) referred to as pneumonitis in the American[4] literature and a discussion of the definition of this term and syndrome ensued. Some of the roentgenographic findings were quite simply typical of lobular (segmental) consolidation and others were consistent with what we now feel can be identified as true virus pneumonitis and bronchopneumonia: a combination of a simple infiltrative processes and minor, even minute, areas of consolidation and partial consolidation. The latter component of this duel process

was frequently subsequent to the former factor and possibly equally dependent on it *and* a secondary invading organism.

As one analyzes more recent reports, the number of infiltrative (pneumonitic) examples has steadily increased until they predominate in the reports of Reimann[14] and constitute a relatively pure subject of discussion for a paper by Smiley, Showacre, Lee and Ferris.[19]

The clinical syndrome has been growing even more uniform both here and in the descriptions of others since 1937 and has been briefly as follows:[8,19]

1. An insidious febrile onset. Progressive regular rise and fall of body temperature without diurnal regularity reaching 103–105° F. after the first day or two.
2. Accompanied by progressive malaise and often severe headache and occasionally severe chest pain.
3. Third or fourth day development of a cough, usually unproductive.
4. Commonly no significant or localized physical finding up to this time and frequently even for some days.
5. Low leukocyte count and negative sputum. A filtrable virus in same groups apparently characterizable by certain animal inoculations which can be duplicated and continued.
6. Early minor, usually centrally located, roentgenographic findings in examination of the lungs by the third to the fifth day.
7. Slowly developing "crescendo" type clinical course: ten to twelve days total elapse of time; followed by decrudescence by lysis, but mild rise in leukocyte count and some productive cough but nonspecific sputum.
8. Or migration of signs, recrudescence of severity and beginning important rise in leukocyte count; probably representing more serious secondary invader.
9. This last mentioned phase is the only one in which sulfonamide drugs appear to be indisputably effective.
10. This process has a definite trend toward contagion as evidenced by familial and other gregarious grouping.

In the past year we have seen 279 reasonably certain cases of primary pneumonia in 221 of which (74 per cent) the history, findings and course have followed the above outline and pattern with remarkable uniformity. The remaining 58 cases encompassed a relatively large group of variable types of primary pneumonic processes. Typical lobar pneumonia with pneumococcus identification has been predominant (42 cases).

Of 254 sputum examinations for pneumococcus identification and typing performed here in the past year, 172 have been negative and some 25 to 35 were positive for types of questionable pathogenicity. This trend seems quite parallel in potentialities to our independent classification of the roentgenologic findings.

DESCRIPTIVE DISCUSSION

Of more interest to us as roentgenologists have been the roentgenographic characteristics of the 221 cases of atypical, possibly virus, pneumonia.

We have come to feel that there are several characteristics of the roentgenographic evidence of this syndrome other than inconstant peculiarities in distribution. In fact, a few of these characteristics seem to be almost exclusive. We, of course, realize that they cannot be considered pathognomonic, since, so far as we know, they do not represent specifically one pathologic process; since, as a matter of fact, we have practically no pathologic material for study. Though the roentgenographic peculiarities of this syndrome do follow the non-lobular, non-segmental and inconstant distribution pattern previously described by many authors, we feel that this distribution pattern is followed in a more or less orderly manner both as to location and as to the progressive chronological development, even of the various "units" in the cases in which they are multiple. We also

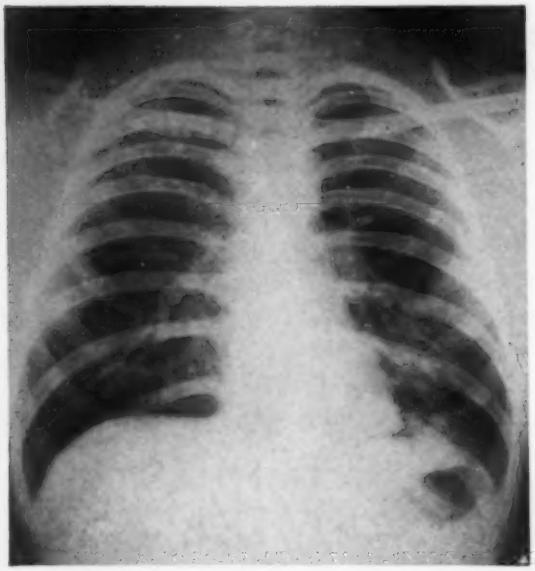


FIG. 1. "Cotton-wool" appearance of centrally located early infiltration and partial consolidation.

feel that a descriptive structural analysis of these processes is characteristic with surprising constancy.

We should like to present our idea of these findings in the following form and offer some pertinent examples as well as examples of some contrasting lesions for standardization (see illustrations). We have found these examples a reasonably constant rule rather than an exception.

1. An infiltrative process at the onset.
   A. First progressively peribronchial from the hilum and then irregularly interbronchial; earlier in the more proximal portion.
   B. Customarily clearly definable as to limits in spite of its disregard for segmental or lobar structural limits, usually involving more than one segment and frequently parts of more than one lobe.

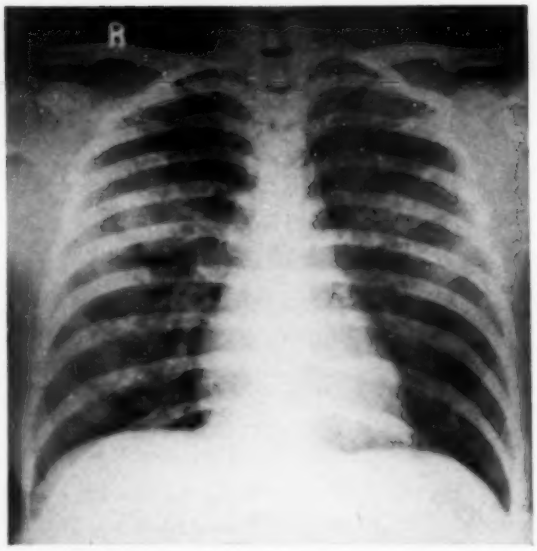


FIG. 3. Early "wire-grass" type infiltration characterizing mid-resolution.

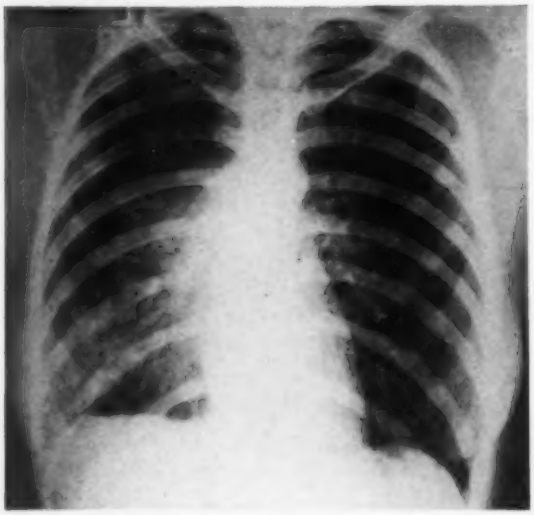
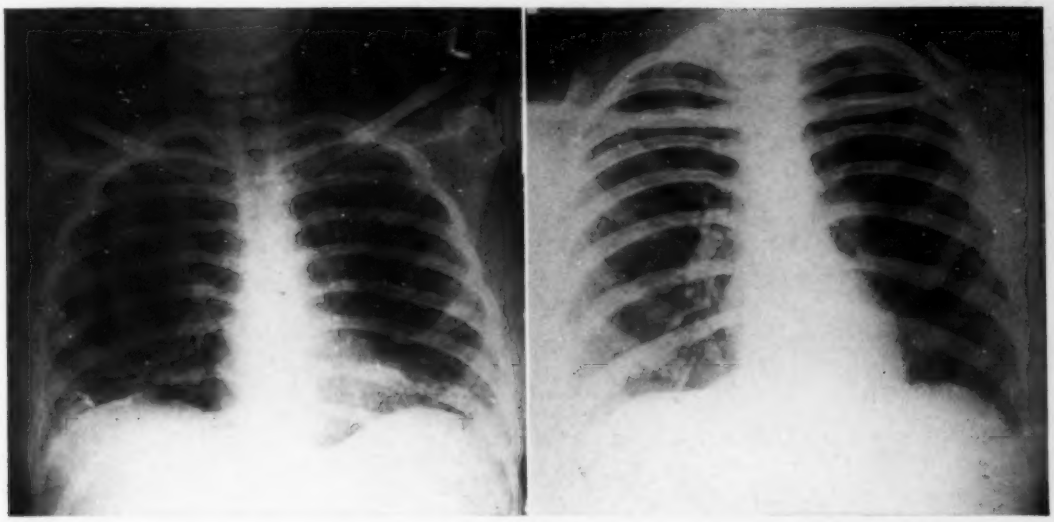


FIG. 2. "Cotton-wool" appearance in so-called inverse phase or resolution with new area or unit developing from right upper hilum.

2. Quickly accompanied by a "cotton-wool" appearance of multiple areas of partial or semi-consolidation.
   A. This is scattered through the area of infiltration; usually distributed in a radial progression also.
   B. Frequently subsequently (six to twenty-four hours) coalescing.
   C. Occasionally eventually (twenty-four to forty-eight hours) filling approximately a whole lobe to simulate lobar pneumonia but, so far as we have seen, always managing to present a striated infiltra-



A *B*

Fig. 4. *A*, late "wire-grass" type infiltration (pseudofibrosis). *B*, same case showing the lungs entirely clear in one week.

tive type background rather than a pure homogenicity.

D. Usually establishing a fixed distribution for any one area in two to three days, which afterward behaves as a "unit."

3. Resolution or absorption begins.
   A. By generalized and uniform progressive (three to five days) loss of density throughout the "unit."
   B. The development of an appearance of "wire-grass" infiltration or

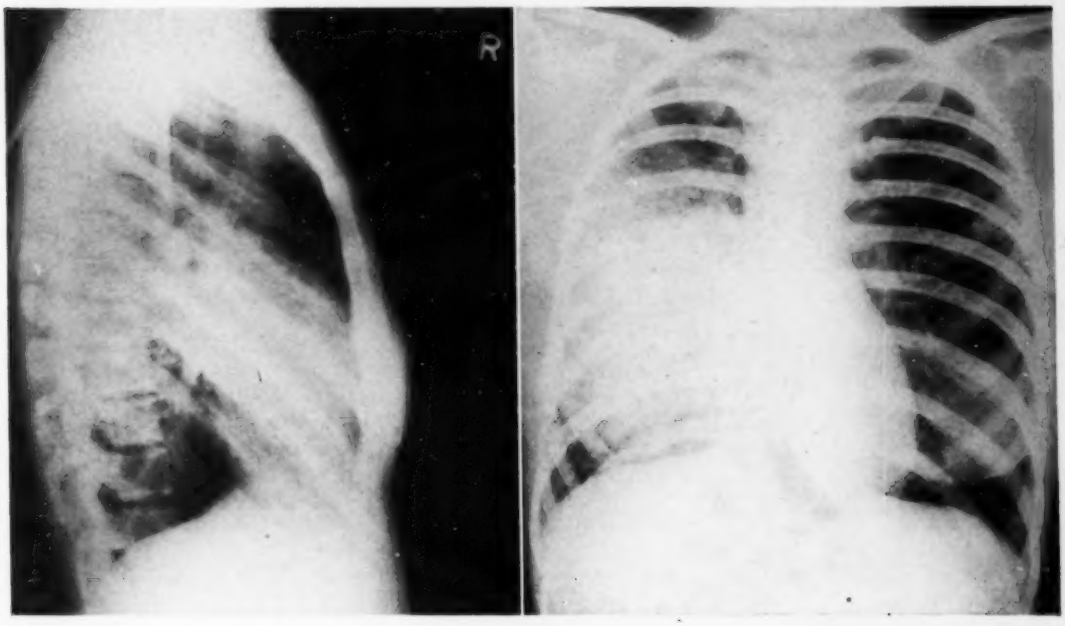


Fig. 5. Extensive distribution simulating lobar pneumonia. Actually the extension is beyond lobar lines and a striated characteristic, mentioned in the text, is retained.

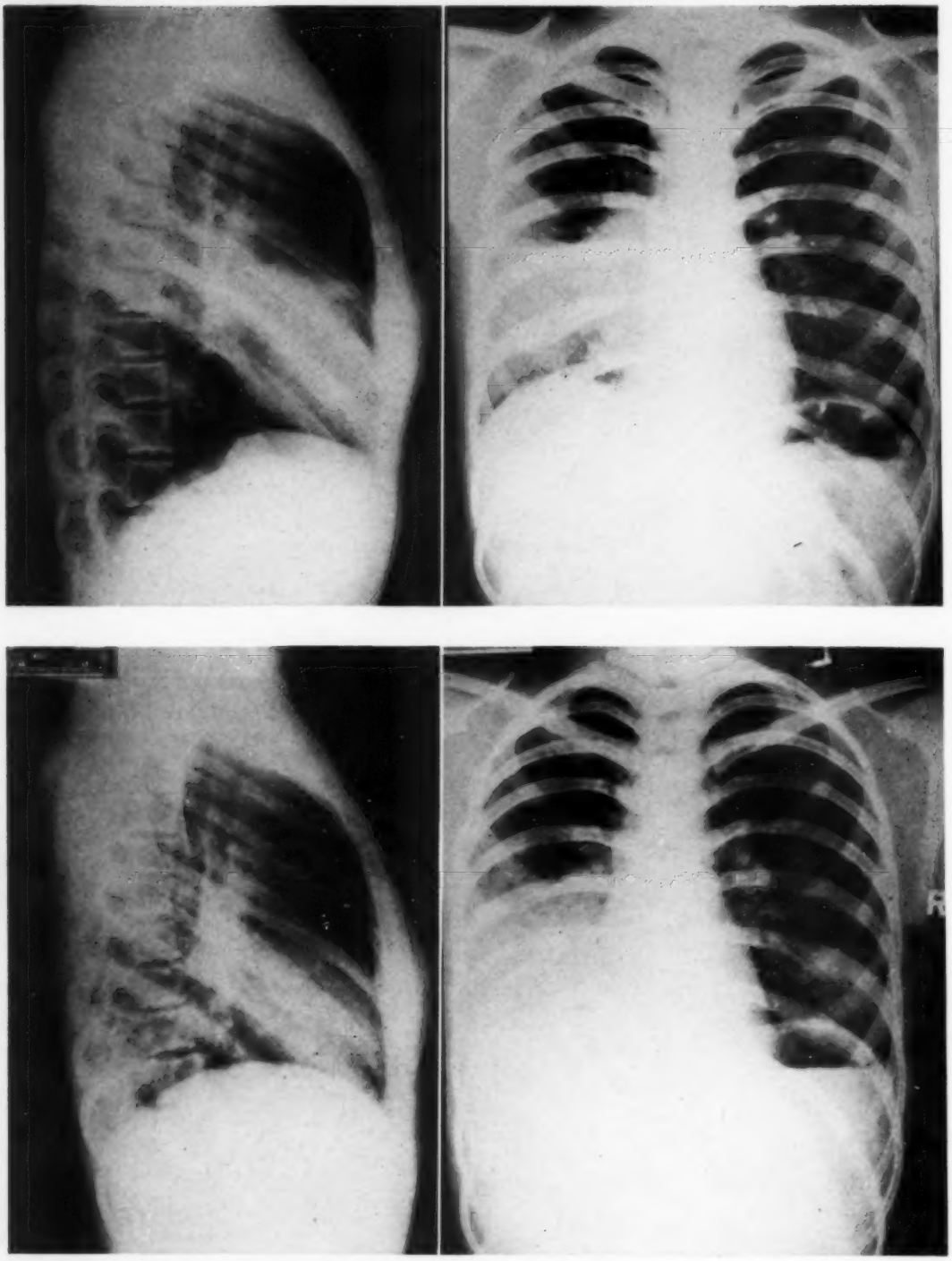


FIG. 6. Two examinations of same patient within forty-eight hours showing (top to bottom) distribution simulating lobar pneumonia but developing lesion characteristics rapidly, indicating a non-pneumococcus process.

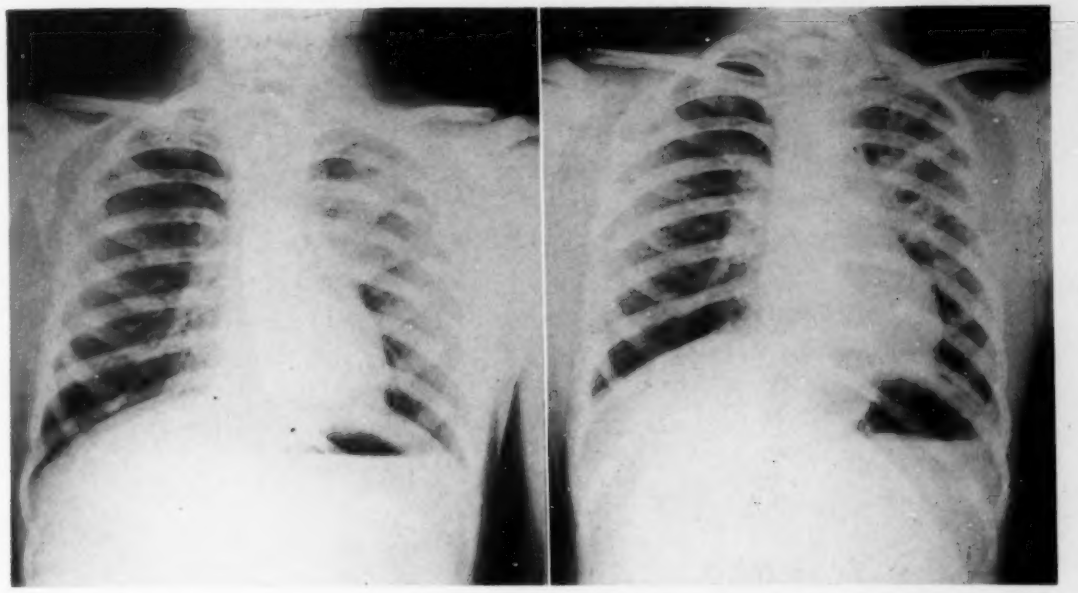


Fig. 7. Typical process and seventy-two hour sequence in seven year old child.

"pseudofibrosis" (suggesting a relatively simple inverse of the developing process).

C. Eventual progressive complete clearing of this process in five to fourteen days, usually five to eight days in cases of single "units."

4. Occasional development of multiple "units" with
   A. Subsequent definite dates of onset and individual chronology.
   B. Rarely, involving nearly all visible parts of lung.
   C. Usually no one unit disturbing the approximate prearranged chronology of any forestarted unit.
5. Occurring quite typically in children.
   A. We recorded only one typical case under six months, but many both under and over two years.

COMMENT

Due to evident difficulty in clinical diagnosis produced by such incipient changes as those which characterize the early onset of this syndrome, we submit that roentgenographic diagnostic procedures have acquired a position of primary importance here. This position, at least for the moment, is in contrast with the recent secondary position of roentgenology in classical lobar pneumonia due to pneumococcus. Naturally, we do not hold with any idea that this syndrome should be expected to maintain a permanent dominant position in the problem of pneumonic processes. Nor do we expect that this degree of uniformity will

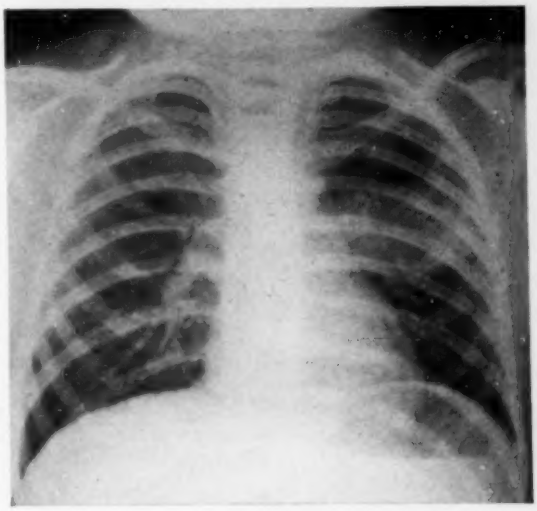


Fig. 8. Typical location, uniform density and definition of lobular pneumococcus pneumonia in a child.

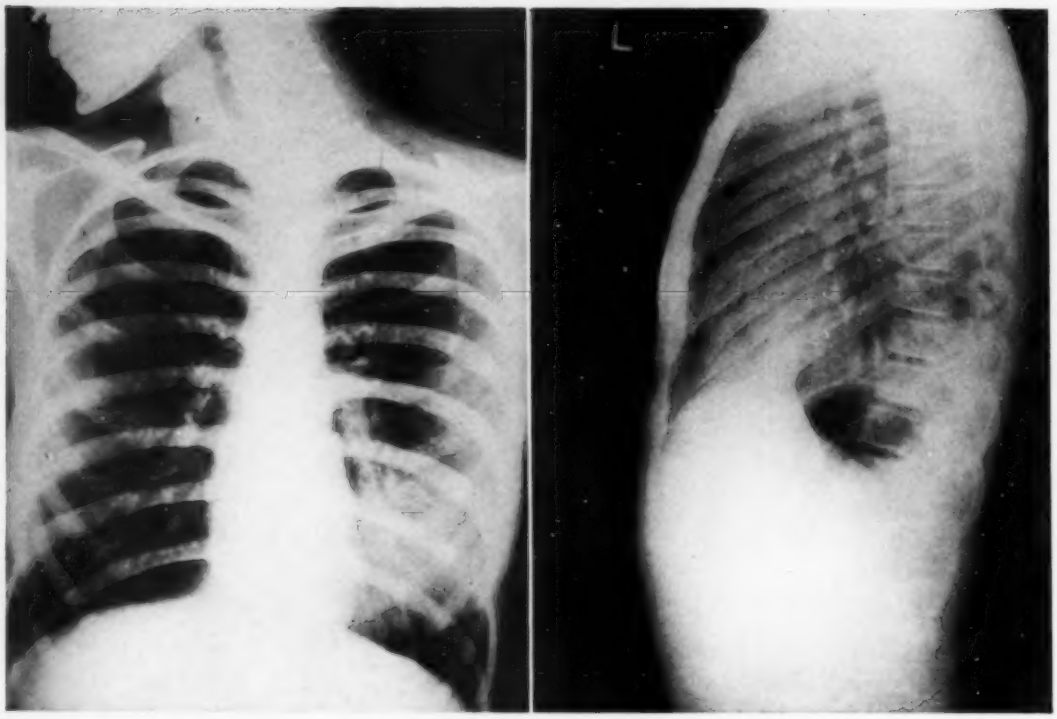


FIG. 9. Typical middle stage (five days after onset) process with typical distribution differing from lobular pneumonia in similar location having similar distribution but different appearance.

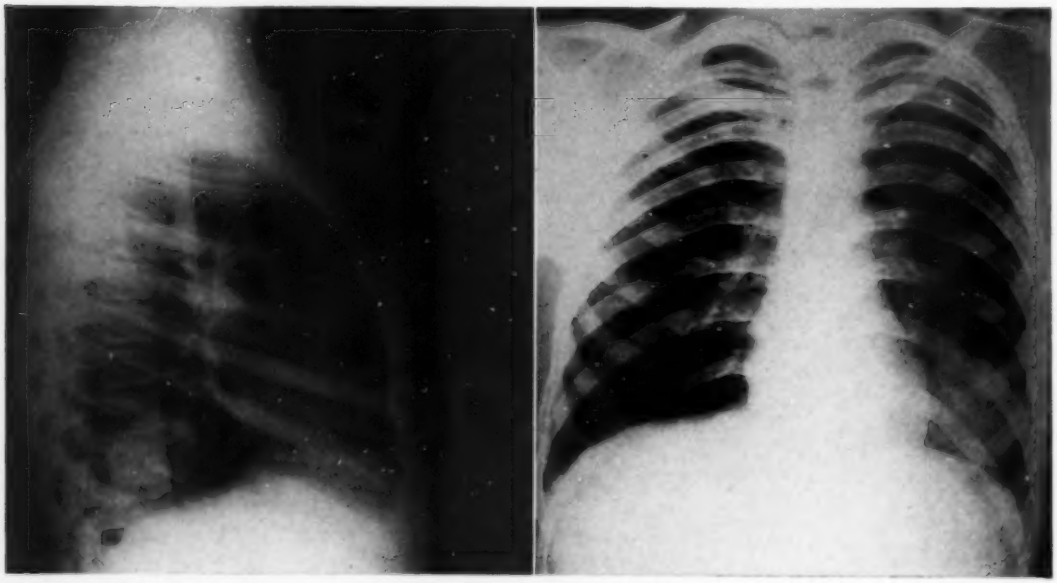


FIG. 10. Characteristic localized segmental or lobular pneumococcus pneumonia of location and size similar to Figure 9.

enjoy widespread geographic distribution. The secondary variants of pneumonia from the pneumococcus have been inconstant in different time cycles and at the same time varied further in separated localities in the same season. We do feel that it represents a currently important cyclic variant of acute pulmonary diseases and is perhaps in the midst of the crescendo of its own importance this year. Nevertheless, it has been gratifying to us to be able to develop some criteria of roentgenographic recognition of this syndrome during the time that it has been so prevalent, and here in the Southwest where it has developed such an apparently pure form. It has been gratifying to find considerable reassurance in the reasonable correlation of findings with other departments. It is paradoxically ungratifying from an academic standpoint to be afforded almost no material for objective verification.

We shall have to rely upon the field of bacteriology to provide eventually a practical and quick means of identifying and subclassifying filtrable virus.

CONCLUSIONS

1. A group of 221 cases of non-lobar (non-pneumococcus) pneumonia have been related and discussed as to certain features. The clinical and laboratory findings correlate well with previously described groups of febrile episodes apparently due at least in part to infection with a filterable virus; possibly one peculiar to this syndrome.

2. We believe that we are able to demonstrate certain pulmonary roentgenologic characteristics of this syndrome over and above "distribution unusual to lobar pneumonia," and inconstancy within its own group.

3. We believe that a remarkably large proportion of these cases follow a fairly constant roentgenologic course, in either single, double, or occasionally multiple chronological "units" or episodes.

4. Staggered concurrence is typical in cases of multiple units.

5. The roentgenologic identification of this entity is important in the face of the common difficulty of establishing dependable clinical identification in typical cases.

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Vol. 49, No. 1

DUODENAL ULCER SYNDROME CAUSED BY ANKYLOSTOMIASIS

REPORT OF TWENTY-FIVE CASES WITH GASTRIC ACIDITY AND ROENTGENOLOGICAL STUDIES*

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GASTROINTESTINAL disturbances caused by hookworm disease may appear in different clinical forms, including that of duodenal ulcer. The symptoms are often vague and indefinite, the patients complaining of heartburn, flatulence, a feeling of fullness of the abdomen and irregular bowel movements. In some cases patients complain of epigastric pain, more marked two to four hours after meals, increased by pressure, but relieved by food and/or alkalis. In localities where ankylostomiasis is very common, dyspepsia associated with severe anemia suggests the diagnosis of hookworm disease. On the other hand, in those countries where hookworm disease is rare, or the infection is light, ankylostomiasis as a cause of painful dyspepsia is often ignored and not considered in differential diagnosis. In those cases where hookworm disease causes symptoms suggestive of duodenal ulcer, a definite diagnosis can be made only by finding ova of *Ankylostoma* in the stools and by roentgenological examination of the gastrointestinal tract with the barium meal.

Ankylostomiasis in Lebanon and Syria, as in many other parts of the world, does not constitute a major public health problem and may be considered of more or less negligible economic and medical importance.[18,25] However, more and more cases are being recognized and its significance from the standpoint of differential diagnosis and treatment is becoming increasingly appreciated.

In the Out-patient Clinics and Hospitals of the American University of Beirut, we have had patients whose clinical history was very suggestive of chronic duodenal ulcer, but in whom stool examination revealed presence of ova of *Ankylostoma duodenale*. These patients have had complete relief from their digestive symptoms soon after the hookworm infestation was cleared. We have noted that some of these patients in whom hookworm disease was associated with painful dyspepsia suggestive of duodenal ulcer gave no history of recent hematemesis or malaria, had severe anemia, microcytic in type. It is a well known fact that painful dyspepsia due to duodenal ulcer is usually associated with high gastric acidity, while hypochlorhydria or achlorhydria is the common finding in anemias. This unexpected association of peptic ulcer syndrome with severe anemia due to hookworm disease prompted us to investigate the gastric acidity and to make roentgenological studies of the gastrointestinal tract of patients with ankylostomiasis. Since etiological relation of gastric acidity to duodenal ulcer and the relation of certain types of anemias to diseases of the gastrointestinal tract is being widely studied at the present time, our observations seemed to us of sufficient interest to be presented in this communication.

Hookworm disease in Syria and Lebanon is confined to certain areas along the coast and to inland districts along the banks of the Euphrates and Orontes Rivers.[3,12,18,25] It is prevalent among gardeners most of whom are poor and uneducated and to

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TABLE I

Case No.	Sex and Age	Chief Complaint and Duration	Free Gastric Acidity	Red Blood Cell Count	Hemoglobin	Roentgen Findings	Complications	Remarks
1	M 25	Epigastric pain ½–2 hr. p.c. Relieved by alkalis not by food; 1 mo. duration	25	3,700,000	70%	Spastic cap, tenderness, exaggerated and reversed peristalsis in duodenum	Blood Wassermann 4 plus; diarrhea	Pain relieved second day after vermifuge. Roentgen examination normal after 17 days
2	M 35	Epigastric pain relieved by food, 2 yr. duration. Dyspnea on exertion	45	2,230,000	30%	Pylorospasm, irritability of descending duodenum. Occasional reversed peristalsis	—	Complete relief of pain on second day after vermifuge. Roentgen recheck 6 mo. later, normal
3	M 41	Epigastric pain 2–3 hr. p.c. relieved by food and alkalis; 6 mo. duration	42	3,700,000	70%	Pylorospasm, tender and irritable duodenal cap. Swelling of mucosa of proximal jejunum	—	Complete relief on second day after vermifuge. Roentgen findings unchanged after 3 days
4	M 21	Epigastric pain 2–3 hr. p.c. Partial relief by food	68	5,430,000	90%	Irritable duodenum, active and reversed peristalsis. Moderate stasis at lower duodenal angle. Swelling of mucosa of proximal jejunum	Amebiasis	Complete relief from pain on second day after vermifuge. Roentgen findings improved 5 days after recheck, normal 8 weeks after vermifuge
5	F 20	Loss of strength and color 9 mo. duration. Heaviness in epigastrium with heartburn	43	1,960,000	20%	Negative	Cardiac dilatation	Roentgen examination normal. No epigastric pain, normal acidity, severe anemia
6	F 18	General weakness	35	2,820,000	45%	Negative	—	Roentgen findings normal. No epigastric pain, normal acidity, marked anemia
7	F 30	Epigastric pain 3–4 hr. p.c. wakes patient at night. Relieved by food and alkalis	33	2,200,000	35%	Negative	Edema of lower extremities	Epigastric pain, although roentgen findings and acidity normal; marked anemia
8	M 28	Heartburn, distention in epigastrium	23	1,890,000	33%	Negative	Pneumonia	Roentgen findings and acidity normal, severe anemia
9	M 30	Epigastric pain rather constant, not relieved by food or alkalis; general weakness	24	4,200,000	70%	Negative	—	Roentgen findings and acidity normal. Epigastric pain not periodic
10	M 36	General weakness, vague abdominal pains for many years	48	3,550,000	50%	Tender and irritable duodenum, active peristalsis	Syphilis, malaria, liver cirrhosis. Wassermann 4 plus	Rather high acidity despite multiple diseases and anemia
11	F 17	Epigastric pain 2 hr. p.c. relieved by food, 2 yr. duration	38	3,750,000	85%	Negative	*B. coli communis* pyelitis	Pain relieved after vermifuge. Roentgen findings and acidity normal
12	F 45	Abdominal pain 5 yr. duration	30	3,550,000	65%	Irritable duodenum	Cholecystectomy 7 yr. duration	Normal acidity with moderate anemia
13	M 45	Epigastric pain 2–3 hr. p.c. Relieved by food and alkalis; 1 yr. duration	87	4,700,000	—	Tender and irritable descending duodenum. Reversed peristalsis	—	Prompt relief after vermifuge. High acidity. Epigastric pain and positive roentgen findings

Table I—*Continued*

Case No.	Sex and Age	Chief Complaint and Duration	Free Gastric Acidity	Red Blood Cell Count	Hemoglobin	Roentgen Findings	Complications	Remarks
14	F 35	Epigastric pain, general weakness, palpitation	94	1,840,000	35%	—	Edema of lower extremities	Severe anemia with very high acidity
15	M 55	Epigastric pain 2 hr. p.c. acid eructations, relief by food and alkalis; 30 yr. duration	62	—	—	Gastric and duodenal mucosa swollen. Reversed peristalsis	Gastroenterostomy, 15 yr. previously, with no improvement	Prompt relief after vermifuge. Operation may have been unnecessary, if correct diagnosis had been made
16	M 22	Epigastric pain 2 yr. duration; heartburn	50	4,390,000	80%	—	*Strongyloides stercoralis*	Prompt relief after vermifuge
17	M 25	Epigastric pain 2–3 hr. p.c. relieved by food and alkalis, of 10 yr. duration	50	4,700,000	85%	Swollen mucosa of cap and descending duodenum. Spastic and tender cap. Increased and reversed peristalsis	Amebiasis; diabetes	Prompt relief after vermifuge. Roentgen findings normal 24 days after vermifuge. Acidity falls 11 points
18	M 23	Epigastric pain 9 mo. duration. Palpitation and dyspnea on effort	85	1,210,000	25%	Pylorospasm, slight broadening of mucosa of cap and descending duodenum. Active and reversed peristalsis. Swelling of jejunal mucosa, barium column tends to be segmented	Cardiac dilatation	Roentgen findings show improvement 5 days after vermifuge. Recheck after 8 mo. normal. Prompt relief of pain after vermifuge. Acidity falls 20 points in 8 mo. *Note:* high acidity with severe anemia
19	M 30	Epigastric pain 4 hr. p.c. relieved by alkalis; 1 yr. duration	63	2,420,000	50%	Slight broadening of mucosa. Irritable duodenum. Active and reversed peristalsis	—	Prompt relief after vermifuge. High acidity with anemia. Roentgen findings normal in 16 days
20	F 14	Loss of strength and color plus fever 1½ mo. duration	33	1,380,000	25%	Irritable cap and decending duodenum. Active peristalsis of stomach and duodenum. Diverticulum of stomach. Slight swelling of jejunal mucosa. Loss of "feathery" pattern	Cardiac dilatation. Edema	Normal acidity. Severe anemia. Roentgen examination shows normal duodenum in 11 days
21	M 16	Abdominal pain and epigastric distention	37	5,000,000	90%	Irritable cap with moderate swelling of mucosa. Increased and reversed peristalsis	*Trichostrongylus*	Prompt relief after vermifuge. Recheck roentgenogram after 10 wk. normal. Recurrence due to complication 4 mo. later. Normal again after 4 wk., vermifuge having been repeated
22	M 45	Epigastric pain and distention after meals	66	4,700,000	85%	Irritable duodenum. Active and reversed peristalsis. Swollen jejunal mucosa. Loss of "feathery" pattern	*Strongyloides stercoralis*, spondylitis, appendectomy 2 yr. before	Relief of epigastric pain after vermifuge
23	M 19	Backache, acid eructations and distention	68	—	—	Slightly swollen mucosa of bulb. Irritable duodenum. Active and reversed peristalsis	—	Digestive symptoms disappeared after vermifuge

TABLE I—*Continued*

Case No.	Sex and Age	Chief Complaint and Duration	Free Gastric Acidity	Red Blood Cell Count	Hemoglobin	Roentgen Findings	Complications	Remarks
24	F 25	Swelling of abdomen and lower extremities 9 mo. duration. Epigastric pain 3–4 mo. duration. Heartburn, loss of strength and color	13	840,000	15%	Slightly swollen mucosa of duodenum and jejunum	Cardiac dilatation, ascites, nephritis	Very severe anemia, cardiac dilatation, circulatory failure, extreme weakness, low free acidity, moderate duodenal changes. Roentgen findings normal 21 days after vermifuge. Iron treatment and diet is followed by rise of red blood cells to 2,580,000 and HCl to 30 within 4 wk.
25	M 35	Epigastric pain 1 hr. p.c. especially after heavy meals. Cough of 12 yr. duration	56	4,730,000	85%	Active gastric and duodenal peristalsis with reversed duodenal peristalsis. Swollen mucosa of duodenum and jejunum	Amebiasis	Prompt relief of pain after vermifuge. Roentgen examination after 12 days shows condition rapidly returning to normal

whom proper medical care is not readily available. During the last few years, however, an increasing number of patients from all walks of life, suffering from hookworm disease, have been examined and treated at this institution.

The present report is based on a series of 25 cases of ankylostomiasis in which, in addition to routine clinical and laboratory studies, gastric juice analysis and roentgenologic studies of the gastrointestinal tract were made. Significant data on all cases are given in Table 1.

Twenty-three out of the 25 patients complained of digestive disturbances and abdominal pain. In 10 cases, epigastric pain had a definite relation to meals, coming on one to four hours after ingestion of food. These patients awoke at night with epigastric pain, pain relieved by intake of food and alkalies. Small quantities of soft and easily digestible food relieved the hunger pains while the intake of coarse food or of large quantities of food increased the epigastric pain and discomfort. In none of these patients was there vomiting, hematemesis or melena. It is significant to note that all patients had relief from epigastric pain and distress within twenty-four hours after administration of the vermifuge (mixture of carbon tetrachloride and oil of Chenopodium). In patients whose pain persisted or returned shortly after administration of the vermifuge, it was noted that ova of *Ankylostoma duodenale* were still present in the stools. A second dose of vermifuge produced complete relief from symptoms.

All 25 patients had positive stools for ova of *Ankylostoma duodenale* upon admission, but the stools became ova free before the patients were discharged. Twenty-three of the 25 patients had roentgenologic examination of the gastrointestinal tract. As many of our patients came from relatively distant sections of the country, it was not possible to obtain on all follow-up roentgenologic evidence of cure.

PATHOLOGICAL CHANGES IN THE SMALL INTESTINE

Although hookworms are most frequently located in the jejunum,[15,18,20,21] they may extend proximally up to the pylorus and distally as far as the cecum and ascending colon. As the name implies, one would expect to find the parasites more abundantly in the duodenum. Their presence in varying levels of the duodenum has been frequently observed.[15,21] The parasites have been recovered from aspirated gastric secretions.[6]

One would assume that the nearer the zone of infection is to the pylorus, with more extensive involvement of the duodenal mucosa, the more likely are the symptoms to simulate those of duodenal ulcer and the more marked the roentgen findings in the duodenum are expected to be.

The pathological changes in the walls of the small intestine are due to the combined effect of the reaction to the trauma inflicted upon the mucous membrane by the formidable hooklets of the parasite, secondary bacterial invasion, as well as the effect of the toxin of the parasite.[18,19,20,21]

There are numerous punctate erosions of the mucosa at the site of attachment of the parasite with varying degrees of hemorrhage into the mucosa and submucosa. Leukocytic infiltration is present and edema of the mucosa is also noted. The findings may be summed up essentially as (*a*) trauma, bleeding and accompanying changes, and (*b*) chronic enteritis.[19]

GASTRIC SECRETIONS

As already mentioned, hypochlorhydria or achlorhydria is the common finding in severe anemias. Our observations are in marked variance with this dictum as can readily be seen from Table 1 and Chart 1, demonstrating a marked rise in free gastric acidity above the normal levels. This is well illustrated by Cases 14 and 18, while Cases 20 and 24, showing the severest degree of anemia observed in any of these cases, still maintain an acidity of 33 and 13 in spite of a red blood cell count of 1,380,000 and 840,000 respectively. To our knowledge no striking findings have hitherto been reported on gastric juice of patients with ankylostomiasis.[2,6,11,24*] Garin, *et al.*[6] and Suárez[24] are of the opinion that neither the number of parasites attached to the duodenal mucosa nor the resulting anemia influence the gastric acidity. They have given no correlation between the degree of acidity and the dyspeptic symptoms.

In Chart 1, curve (*1*) represents the free acidity curve plotted from 10 cases of ankylostomiasis with symptoms indicative of duodenal ulcer and with positive roentgen findings in the duodenum. It is higher than the curve for duodenal ulcer. Curve (*2*) is plotted from all the remaining cases of ankylostomiasis reported in this series, other than the 10 already referred to. It is similar to curve (*3*) which is plotted from free acidity curves of 50 cases of active duodenal ulcer, before treatment, at the American University Hospitals. Curve (*4*), representing a normal level, is based on the free acidity curve of 100 healthy medical students at the University, who are known to be free of ankylostomiasis, or other disease.

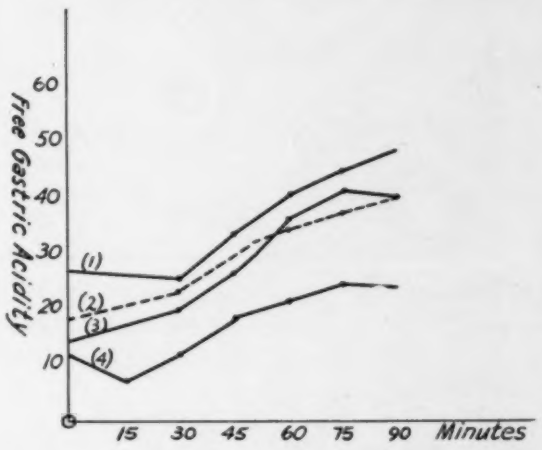

Chart 1. (*1*) free acidity curve plotted from 10 cases of ankylostomiasis with symptoms of duodenal ulcer and positive roentgen findings; (*2*) free acidity curve plotted from all remaining cases; (*3*) free acidity curve of 50 cases of active duodenal ulcer before treatment; (*4*) free acidity curve of 100 healthy medical students.

ROENTGENOLOGIC OBSERVATIONS

The occurrence of duodenal irritation and duodenal inflammation in the absence of a peptic ulcer is gaining wider recognition in the fields of pathology and clinical medicine as well as of roentgenology. Discussion of this subject is outside the realm of this paper and will be considered elsewhere. Roentgenologic studies of the gastroin-

* Since this paper was read references 2 and 11 have appeared.

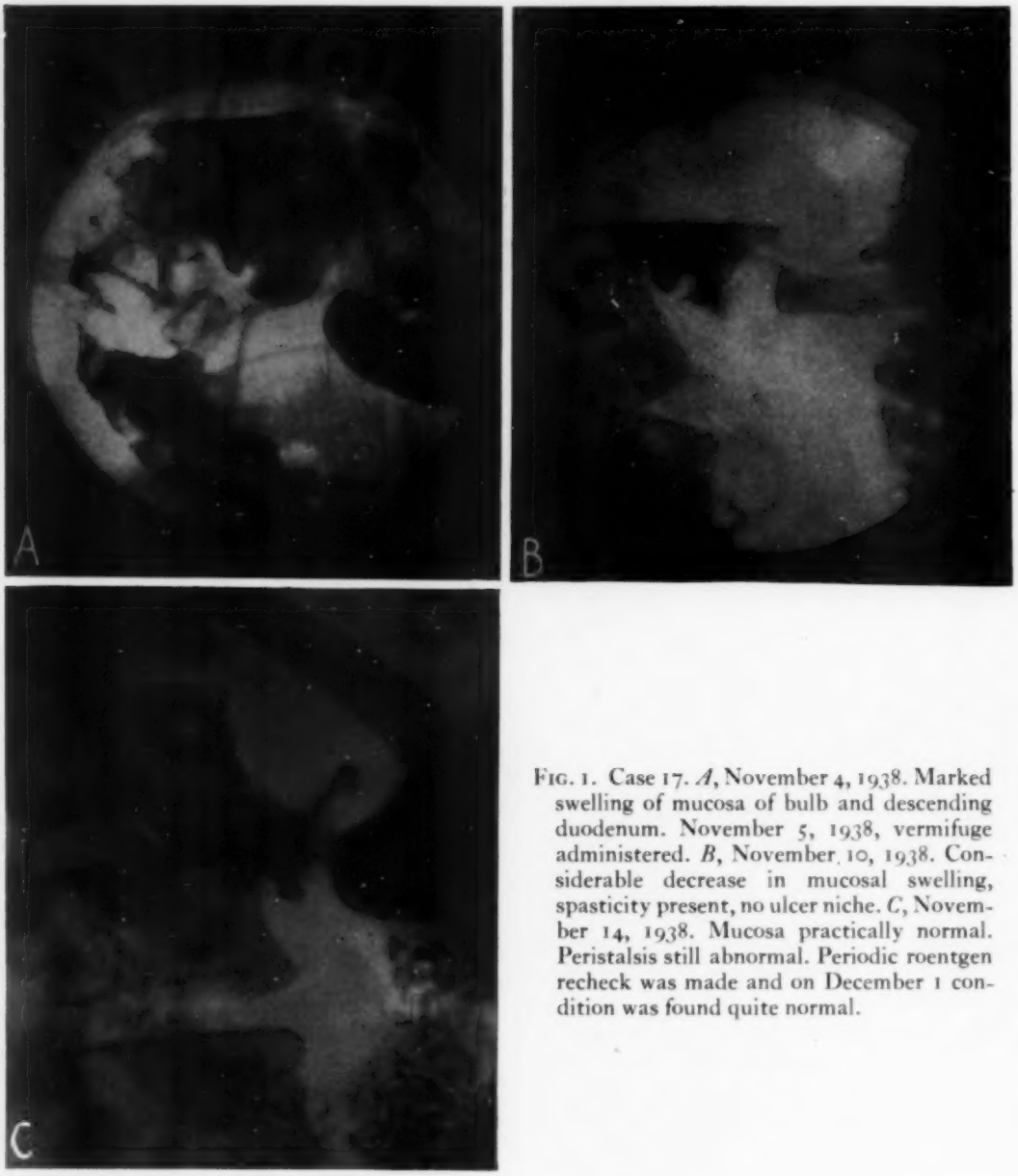

FIG. 1. Case 17. *A*, November 4, 1938. Marked swelling of mucosa of bulb and descending duodenum. November 5, 1938, vermifuge administered. *B*, November 10, 1938. Considerable decrease in mucosal swelling, spasticity present, no ulcer niche. *C*, November 14, 1938. Mucosa practically normal. Peristalsis still abnormal. Periodic roentgen recheck was made and on December 1 condition was found quite normal.

testinal tract of patients with ankylostomal infection reveal, in the majority of cases, certain findings which indicate the presence of definite irritability or inflammation of the duodenum, and sometimes of the jejunum. This varies in degree and location and most probably depends on the severity of the parasitic infestation as well as on the part of the intestines that is most involved.

Of the 25 cases under consideration, 23 were examined roentgenologically. Of these, 17 cases, or 68 per cent, showed definite roentgenologic changes in the duodenum. These changes may be divided into functional and anatomical.

The stomach often presents the same roentgenologic aspects seen in association with a duodenal ulcer or duodenitis. Peristaltic activity is increased and gastric evacuation is accelerated. At times, slightly prolonged initial pylorospasm is observed.

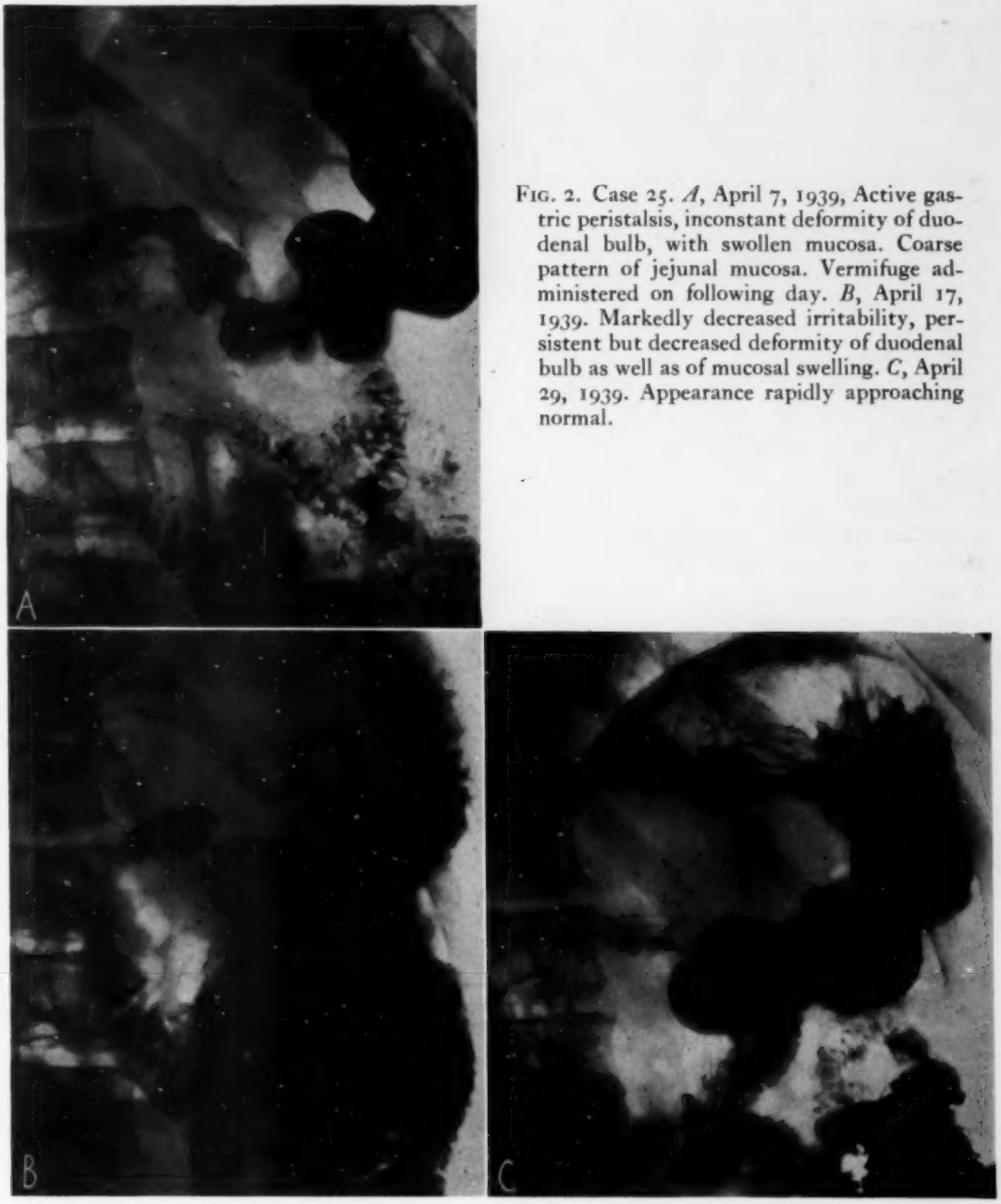

Fig. 2. Case 25. *A*, April 7, 1939, Active gastric peristalsis, inconstant deformity of duodenal bulb, with swollen mucosa. Coarse pattern of jejunal mucosa. Vermifuge administered on following day. *B*, April 17, 1939. Markedly decreased irritability, persistent but decreased deformity of duodenal bulb as well as of mucosal swelling. *C*, April 29, 1939. Appearance rapidly approaching normal.

As the functional changes are the ones most constantly observed, the roentgenoscopic part of the examination is all the more important. Roentgenographic records are of diagnostic value when definite changes in the mucosa are demonstrable.

Functional Changes. These may be motor and secretory.

The duodenum as a whole is irritable. The contrast medium is carried rapidly forward by active peristalsis. Often reversed peristalsis sends the barium backwards, moving it back and forth several times, producing a "pendulum effect." This latter finding is not constantly present, may be observed less commonly in normal patients, and cannot be considered diagnostic. In this connection, our findings are at vari-

ance with those reported by other observers[9,10] who consider this sign of great diagnostic significance. Reversed peristalsis was found in 12 of the 23 cases roentgenologically examined. Varying degrees of spasticity of the duodenal bulb are observed. Mild transitory stasis at the lower duodenal angle is noted at times.

Repeated roentgenoscopic observations at frequent intervals after the administration of antihelminthics demonstrates a steady decrease in the intensity of these signs as the duodenum gradually returns to normal.

No gastric retention has been observed. Increased secretion in the stomach and duodenum tends to decrease the density of the contrast medium. Tenderness is elicited on pressure over the duodenum, especially over the bulb when the latter is involved. The epigastrium is also tender on pressure.

Anatomical Changes. Varying degrees of swelling of the mucosa with alteration of its pattern was observed roentgenologically in 8, or 31 per cent, of the cases (Fig. 1 and 2). The occurrence of spasticity together with swelling of the mucosa and accompanying deformity of the duodenal bulb renders differential diagnosis from ulcer difficult.

The absence of a definite niche, the inconstancy of the deformity and the rapid return to normal after the administration of a vermifuge eliminates every doubt as to whether there had been an ulcer or a nonparasitic duodenitis. After the administration of the vermifuge, these patients were allowed their regular diet. Thus it is not possible to attribute any of the improvement so obtained to the effect of a special dietary regimen. In certain instances, the finding of ova of *Ankylostoma* in the stools may be the only means of differentiation between an ankylostomal duodenitis and a non-ankylostomal duodenitis or a condition with marked irritability of the duodenum.

This is mentioned to emphasize the fact that although the above described roentgenoscopic and roentgenographic findings, when present, are typical in ankylostomal infection, they are by no means characteristic or pathognomonic of the condition.

In the jejunum, alterations from the normal were occasionally met with in these cases. The usual "feathery" appearance of the contrast medium in the jejunal loops is lost, the pattern is coarse, and the mucosa is swollen. At times, in later stages, the contrast medium tends to appear in more or less isolated solid columns or masses. It is not possible to evaluate the significance of this finding in the light of changes due to vitamin deficiency when so few observations have been made.[8,16,23*]

Following the administration of antihelminthic treatment, the patient's symptoms cleared up almost immediately, pain usually disappearing by the second day. Roentgenologically the return to normal is much slower. Although localized tenderness is the first sign to disappear, roentgen evidence of duodenitis and duodenal irritation remains for some time, and if unduly persistent, is an indication of continued infection or reinfection.

Only after a thorough and effective treatment, with repeated negative stool reports, may a cure be assumed. Roentgenological confirmation of a cure is usually obtained in from eleven to twenty-four days after the administration of the vermifuge. Evidence of improvement, both roentgenoscopic and roentgenographic, is apparent as early as the third to the fifth day.

In some cases it was not possible to make a roentgenologic re-examination until a few weeks or months had elapsed. It is not to be inferred that such a long time was needed for a cure. It means that the patients were late returning for their re-examination, while a few never came.

Of the 17 cases with positive roentgenological findings in the duodenum, 4 had a normal gastric acidity, 2 were in the limits of high normal, 8 had definite hyperchlorhydria, and 3 a "towering" high free acidity. The latter 3 were 87, 94 and 85 respec-

* Since this paper was read references 8 and 16 have appeared.

tively, the last 2 having red counts of 1,840,000 and 1,210,000 respectively. Ten cases had a severe anemia varying between 800,000 and 2,820,000 red blood cells per cubic millimeter.

Four had epigastric pain which had no definite relation to meals. Ten had symptoms highly suggestive or indicative of peptic ulcer, pain coming on from one to three hours after meals, relieved partially or completely by food or alkalies or both. On the other hand, 2 cases with symptoms suggestive of duodenal ulcer had normal gastric acidity and a normal duodenum by roentgen examination.

We feel that these studies have a direct bearing on the problem of differential diagnosis and treatment of patients complaining of symptoms of, or symptoms simulating a duodenal ulcer.

Although ankylostomiasis is not frequent in this country, after reviewing these cases it seems desirable to keep it in mind, especially where patients have such different and varied occupations and come from such different classes of society.

Most gratifying results may be obtained through a correct etiologic diagnosis followed by an effective and specific treatment. Compare, on the one hand, a patient with an ankylostomal duodenitis with another who has a non-ankylostomal duodenitis or duodenal ulcer. Both patients present essentially similar symptoms.

The former is relieved of symptoms on the second day after the administration of the vermifuge and is completely cured in from eleven to twenty-four days.* The patient's activities are limited only during the period when the vermifuge is administered, after which normal activity and diet are resumed. On the other hand, a patient suffering from a non-ankylostomal duodenitis or a duodenal ulcer will require a prolonged expensive and strict dietary regimen and in most cases the patient's activities are restricted for a relatively longer period.

* It is evident that "cure" refers to the condition of the duodenum and accompanying signs and symptoms. Severe anemia and other complications accompanying long-standing and severe infections present aspects of the disease not under consideration in this paper. Such conditions did not come up for primary consideration in this series of cases.

CONCLUSIONS

Gastrointestinal disturbances caused by hookworm disease may produce symptoms closely simulating duodenal ulcer.

Estimation of free gastric acidity shows a rise to a level higher than that obtained in duodenal ulcer. In spite of varying degrees of severe anemia, such a high gastric acidity is maintained. Roentgenological studies of these cases show evidence of swelling of the duodenal mucosa, inconstant deformity of the duodenal bulb (duodenitis without ulcer niche), hyperperistalsis of stomach and duodenum, and, commonly, reversed peristalsis of the duodenum without obstruction. Administration of a vermifuge successfully results in the elimination of epigastric pain within twenty-four hours, and the restoration of the duodenal wall in from eleven to twenty-four days.

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DEVELOPMENT, CLINICAL MANIFESTATIONS, AND TREATMENT OF RHEUMATOID ARTHRITIS OF THE APOPHYSEAL INTERVERTEBRAL JOINTS

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I. OBJECT OF STUDY

IN ANALYZING diseases which are grouped with arthritis of the spine, it is useful to make a distinction between lesions of the vertebral symphyses and lesions of the apophyseal joints. The name *vertebral symphysis* is used in this paper to designate the articulation between two vertebral bodies and the intervening vertebral disc, since this junction is a synchondrosis or symphysis like the pubic symphysis.[1] The *apophyseal joint*, which connects contiguous articular processes, is a synovial or diarthrodial articulation like the joints of the limbs. This anatomical difference has its clinical significance. Previous observations suggested that the mobility of the spine depends on the integrity of the apophyseal joints rather than on the condition of the vertebral symphyses and ligaments.[16,19] In continuation of these studies a group of patients has been examined in whom severe stiffness of the back or neck was present, together with other variable symptoms conforming to the clinical picture of Strümpell-Marie disease or rhizomelic spondylosis. The anatomical lesion associated with this syndrome is quite distinctive, but has been variously interpreted, e.g., as a decalcification of bone followed by ossification of fibrous tissue,[12] a syndesmotic type of spondylitis;[24] an ossifying disease of the vertebral ligaments;[9] an atrophic spondylitis;[7] or an ankylosing arthritis of the apophyseal joints.[5,16,24] All of these theories are based upon postmortem findings. But since "one does not die from rhizomelic spondylosis,"[12] autopsy usually discloses only the advanced stages during which the primary lesion is almost invariably overgrown by reparative or incidental changes. Hence the pathology of the initial lesion is not yet sufficiently known, and these anatomical findings do not explain adequately the clinical manifestations which were present during earlier stages. In order to correlate clinical and anatomical findings it is necessary to compare the clinical manifestations present at any one time with the lesion that is present at the same time. If, from a study of these correlations, we could learn to recognize the anatomic lesion in its incipient phase, we may hope perhaps to treat more effectively this disease which has hitherto been incurable because its diagnosis is usually made at an advanced stage, when restitution to the normal can no longer be expected. On the basis of observations about the gradual evolution of the clinical and of the corresponding anatomical pictures, the attempt is made in this paper to answer three questions:

1. In which part of the vertebra is the primary lesion localized and of what nature is it?
2. What produces the characteristic stiffness of the back and neck present in this disease?
3. Can treatment be directed by the findings?

II. METHOD

Fifty patients with severe stiffness of the back and/or neck, and with other variable symptoms, were examined during the years 1934–1941; 12 of them at least twice at different intervals. The findings were compared with those of two control series: (1) 50 patients with stiffness of back and/or neck not caused by vertebral disease; (2) 50 patients with lesions confined to the vertebral symphyses, with or without clinical symptoms. In addition to

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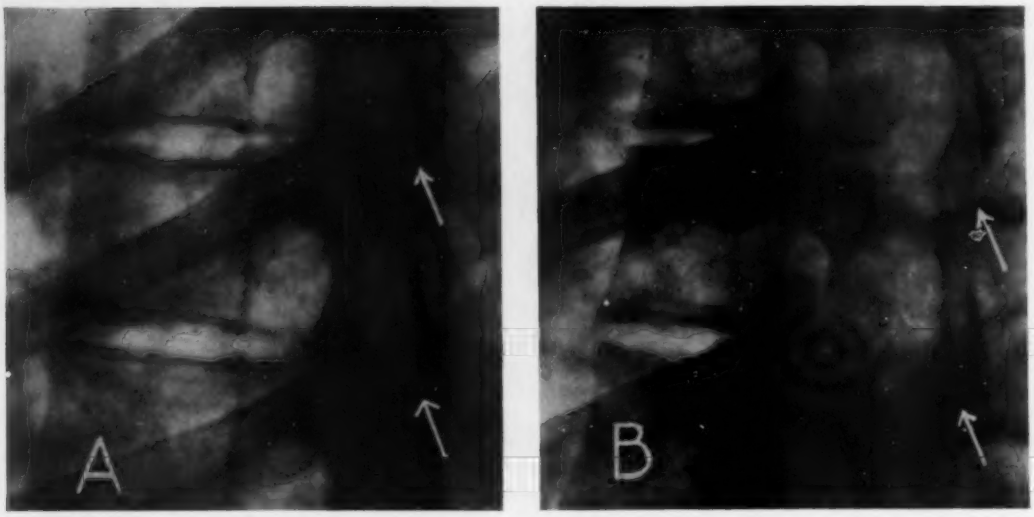

FIG. 1. A picture falsely suggestive of a lesion is produced by a slight technical inaccuracy. Thoracic spine of a healthy woman aged twenty-one. *A*, correct incidence at an angle of 18°. Joints normal (arrows). *B*, deviation of 4° from the position shown in *A* renders the joint spaces invisible, thereby suggesting ankylosis (arrows).

physical and laboratory examinations a study of vertebral movements was made in every case and was recorded on photographs, roentgenograms, or both, in 39 patients of the first group, and in 42 cases of the two control series. Roentgenograms were always made of the entire spine, regardless of the seat of symptoms. The

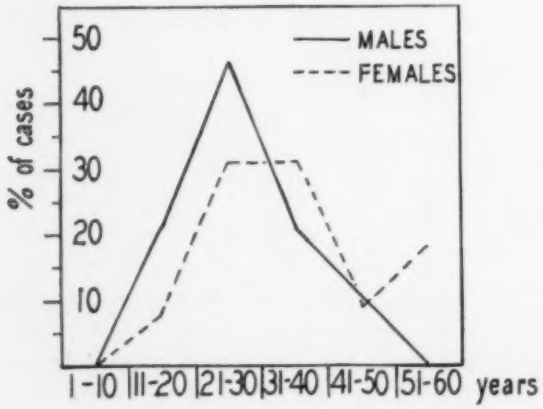

FIG. 2. Age distribution of onset of vertebral symptoms.

technique has been previously described.[16] Accurate positioning is necessary. Since the facets of the articular processes vary in direction[8,11,16] the findings have to be verified in many cases on roentgenograms repeated at slightly different angles. Deviations from the angle required in the individual case may result in appearances falsely suggestive of ankylosis (Fig. 1). Owing to the general limitations of roentgen interpretation some findings remain ambiguous even after several examinations; 5 such cases have not been included in this report.

III. INCIDENCE AND DISTRIBUTION

The 50 cases represent 3.2 per cent of all vertebral lesions observed between 1934 and 1941 in the Department of Roentgenology of the American University Hospitals, Beirut. Twelve of the patients were female (24 per cent). Both the total incidence and the percentage of female cases are greater than reported by other writers.[6,9,11,20] Although the roentgen technique used in our series discloses slight and incipient lesions which cannot always be shown on conventional roentgenograms,[16] this can hardly account for the relatively large number of cases observed in Beirut, since, using the same technique, I found that in Europe and in the United States these cases total 0.9 and 1.1 per cent re-

spectively of all vertebral lesions which I examined.

The age distribution (Fig. 2) shows a peak for the onset of symptoms in the second decade. The tendency to onset at a slightly later period in women, as seen on the graph, corresponds to the observation that all types of arthritis begin later in women than in men.[20] The onset of symptoms other than vertebral has not been taken into account here. The "prespondylitic" manifestations[6] ranged from recurrent muscle ache to severe arthritis of peripheral joints; but their real nature could not always be inferred from the histories or clinical data.

IV. ETIOLOGY

The histories and findings failed to suggest tangible etiologic factors in 22 instances. For the remaining 28 patients (56 per cent) the probable etiology is presented in Table 1.

Column 1 includes patients with a gonorrheal infection which preceded the onset of vertebral or articular symptoms by not more than four months, as well as patients with chronic gonorrhea proved bacteriologically. Three cases with a history of neisserian infection are not included because of an interval of over four years between infection and onset of symptoms, in the absence of chronic gonorrhea. Four other patients acquired gonorrhea several years after the onset of vertebral pain. Of the 2 persons with a history of trauma, column 2, one had fallen onto his back from a height of about 12 ft., the other had been severely beaten on the back. Both stated, and witnesses confirmed, that pain and stiffness of the back began within one week after the trauma. This unusual etiology was also recorded by Pierre Marie in one instance.[14] Under the heading "exposure," in column 3, patients are listed who, prior to the onset of symptoms, had been working barefooted in irrigated fields during winter, or had been flooded, trapped in snow, or the like. Two such cases are not included, being presented in column 4 because they developed rheumatic fever immediately after an exposure of this kind. In the patients of column 4, with rheumatic fever, the vertebral disease was preceded by pain and swelling of several peripheral joints and fever of not less than five weeks' duration; in 3 of these cases, one or several peripheral joints were still swollen, and body temperature was still elevated, at the time when the spine was examined. The cases classified under the heading "chronic sinus," in column 5, form a distinct group with findings, apparently not yet described, to be reported separately.* In these patients the vertebral lesion was confined to spinal segments located at the level of a chronic discharging lesion of the soft tissues of the back or neck. For instance, in a patient who had suffered from recurrent carbuncles of the neck for about five years, only the cervical vertebrae were involved. In the other cases the lumbar vertebrae were found diseased in that region in which the soft tissue lesion was located. Since there were no signs of vertebral tuberculosis, nor of a macroscopic connection between the spine and the fistula, it was assumed that the vertebral lesion was not the cause, but the result, of the soft tissue lesion, in analogy to the ankylosis of the wrist joint which sometimes develops as a sequela of whitlow of a finger tip.[13]

Table I

CAUSE OF THE CONDITION

1 Gonorrhea	2 Trauma	3 Exposure to Cold	4 Rheumatic Fever	5 Chronic Sinus
10=20%	2=4%	3=6%	9=18%	4=8%

Foci of infection in the teeth, tonsils, or paranasal sinuses were noted in 6 patients of the rheumatic fever group. Sundry other infections, such as chronic malaria, recurrent cystitis, amebiasis, were present in

* Oppenheimer, A. Paravertebral abscesses associated with Strümpell-Marie disease. *J. Bone & Joint Surg.*, January, 1943.

TABLE II

SYNOPSIS OF FINDINGS

Case No. (X-ray No.)	Age Sex	Duration of Vertebral Symptoms	Stage	Involved Region	Apophyseal Joints			Vertebral Bodies	Discs	Ligaments†			Joints of Trunk and Limbs				Pubic symphysis	Pain		Rigidity
					Articular processes	Facets	Joint space			Longitudinal	Flava	Spinous	Costovertebral	Sacroiliac	Hips	Limbs		Local	Radicular	
1 (6- 805)	45 m	12 days	I	L III/IV	rarefied	eroded	narrow	normal	normal	−	−	−	normal	normal	normal	normal	normal	+	−	+
2 (8-2240)	27 m	3 mo.	I	L II/III III/IV	raref.	eroded	narrow	normal	normal	−	−	−	normal	eburnat., narrow	normal	normal	normal	+	−	+
3 (8-2934)	28 f	20 days	I	L II/III	raref.	eroded	narrow	normal	normal	−	−	−	normal	blurred	normal	normal	normal	+	−	+
4 (8-2950)	35 f	2 yr.	I	C V, L II/III	raref.	normal?	narrow	normal	normal	−	−	−	normal	normal	normal	normal	normal	+	+	+
5 (9- 905)	35 m	3 mo.	I	L IV/V	raref. ++	invis. (raref.)	narrow	normal	normal	−	−	−	normal	normal	normal	normal	normal	+	+	+
6 (8-3510)	39 m	5 yr.	II	C D L	normal	rough	narrow	normal	normal	(+)	((+))	+D	rough	(ankyl.)	normal	normal	normal	−	−	+
7 (8-1723)	54 m	16 yr.	II	C D L	normal	rough; circl.*	narrow	normal	normal	(+)	(+)	(+)	normal	ankyl.	normal	normal	normal	(+) neck	−	+
8 (5- 156)	30 m	5 yr.	II	L	raref.	ragged, some ankyl.	narrow	raref.	normal	−	+	(+)	normal	ankyl.	normal	normal	normal	+	+	+
9 (6-1406)	30 m	3 yr.	II	C D L	raref.	eroded	narrow	raref.	normal	−	−	−	normal	ragged	normal	normal	normal	+	−	+
10 (7-1901)	35 m	7 yr.	II	D L	(raref.)	ragged	normal	(raref.)	normal	+L	−	+D	normal	ragged	normal	normal	normal	+	−	+
11 (8- 254)	45 f	10 yr.	II	C L	(raref.)	eburnated	very narrow	(raref.)	normal	−	−	−	rough	ankyl.	L ankyl.	knees	normal	+	−	+
12 (8-2788)	60 f	8 yr.	II	C L	raref.	ragged	narrow	raref.	normal	−	−	−	normal	almost ankyl.	narrow	normal	normal	+	−	+
13 (8-2795)	37 m	9 yr.	II	C D L	raref.	D ankyl.	narrow	raref.	normal	−	−	−	rough	ankyl.	normal	normal	normal	(+)	−	+
14 (9- 205)	15 m	2 yr.	II	L	raref.	rough	very narrow	raref.	normal	−	−	−	normal	(ankyl.)	narrow	normal	normal	+	−	+
15 (9-2671)	28 m	15 days	II	L	(raref.)	eroded	very narrow	(raref.)	normal	+	−	−	normal	normal eburnat.	normal	normal	normal	+	−	+
16 (8-1390)	35 m	2 yr.	II	C D L	dense	circl.*	very narrow	normal	normal	−	−	−	normal	ankyl.	normal	normal	normal	+	+	+
17 (8- 390)	41 m	5 yr.	II	C D L	raref.	eroded, eburnated	very narrow	raref.	normal	−	−	−	normal	(ankyl.)	normal	normal	normal	+	−	+
18 (6-1568)	57 f	5 yr.	II	C D L	normal	rough	very narrow	(raref.)	normal	+	−	−	normal	normal	narrow	knees, hands, feet	normal	+	+	+
19 (5-13703)	30 f	2 yr.	II	L	normal	rough	very narrow	normal	normal	+	+	−	normal	(ankyl.)	normal	normal	normal	+	−	+
20 (7-2114)	16 m	1½ yr.	II/III	C_{++} L_{+}	raref.	eroded	almost gone	raref.	normal	−	−	−	normal	eburnated, ragged	normal	normal	normal	+	−	+
21 (7-1993)	35 f	7 yr.	II	C_{++} D L_{+}	raref.	eroded	almost gone	raref.	normal	+	−	(+)	normal	(ankyl.)	(ankyl.)	normal	normal	+	−	+
22 (8- 789)	20 m	3 yr.	II	D L	raref.	eroded	narrow	raref.	normal	−	−	−	rough	eburnated, ragged	normal	normal	normal	+	+	+
23 (9-1621)	40 m	4 yr.	II	L	normal	circl.*	narrow	normal	normal	−	−	−	normal	eburnated, ragged	normal	normal	normal	+	−	+

The parentheses indicate that the change in question is of a moderate degree.
* circl. = circling ankylosis. † the sign, −, means that the ligaments are not visible; the sign, +, means that the ligaments are ossified.

24 (9-1883)	19 m	2 yr.	II	C L	raref.	eroded, circl.*	very narrow	raref.	normal	−	−	−	normal	ragged	narrow ragged	normal	normal	+	+	+
													(ankyl.)	ankyl.	(ankyl.)	All periph.	raref.			

The parentheses indicate that the change in question is of a moderate degree.
* circl. = circling ankylosis. † the sign, —, means that the ligaments are not visible; the sign, +, means that the ligaments are ossified.

24 (9-1883)	19 m	2 yr.	II	C L	raref.	eroded, circl.*	very narrow	raref.	normal	—	—	—	normal	ragged	narrow ragged	normal	normal	+	+	+
25 (8-3240)	38 f	6 yr.	II	C D L	raref.	eroded	narrow	raref.	normal	(+)	+	+	(ankyl.)	ankyl.	(ankyl.)	All periph. joints	raref.	+	—	+
26 (7-2909)	36 m	7 yr.	II	C D L	raref.	eroded, circl.*	very narrow	raref.	normal	+	—	—	(ankyl.)	ragged cond.	(ankyl.)	normal	raref.	+	—	+
27 (8-1806)	50 f	12 yr.	II	C D L	raref.	ragged	very narrow	raref.	normal	+	—	—	(ankyl.)	ragged	(ankyl.)	normal	raref.	+	—	+
28 (8-2683)	65 m	10 yr.	II	L	raref.	ragged	very narrow	raref.	normal	(+)	—	—	normal	normal	(ankyl.)	normal	normal	—	—	+
29 (8-3750)	39 m	14 yr.	II	L	dense	rough, circl.*	very narrow	normal	normal	—	(+)	—	normal	ankyl.	(ankyl.)	normal	normal	+	—	+
30 (7- 469)	35 m	4 yr.	III	L		ankylosed		normal	normal	+	+	—	normal	ragged	(ankyl.)	normal	normal	—	—	+
31 (9-1438)	32 m	9 yr.	III	D L		(ankylosed)		normal	normal	+	+	—	ankyl.	ankyl.	(ankyl.)	normal	normal	+	—	+
32 (8- 620)	25 m	3 yr.	III	D L		ankylosed		raref.	normal	—	—	—	normal	ragged	(ankyl.)	normal	normal	+	—	+
33 (7-1436)	36 m	6 yr.	III	D L		ankylosed	circl.*	raref.	normal	+	+	—	ankyl.	(ankyl.)	(ankyl.)	normal	normal	+	—	+
34 (3-9407)	24 m	2 yr.	III	D L		ankylosed		normal	normal	(+)	—	—	ankyl.	(ankyl.)	(ankyl.)	knee	normal	+	—	+
35 (8-1114)	30 m	3 yr.	III	D L		ankylosed		normal	normal	(+)	+	—	normal	ankyl.	(ankyl.)	normal	normal	+	+	+
36 (8-2207)	27 m	3 yr.	III	L		ankylosed		raref.	normal	+	—	—	normal	ankyl.	(ankyl.)	normal	normal	+	+	+
37 (8-2367)	60 m	42 yr.	III	C D L		ankylosed		normal	normal	+	+	+	(ankyl.)	ankyl.	(ankyl.)	normal	normal	—	—	+
38 (8-2773)	38 m	2 yr.	III	C D L		ankylosed		normal	normal	+	+	+	ankyl.	ankyl.	(ankyl.)	knees, should.	raref.	+	—	+
39 (8-3175)	38 m	6 yr.	III	C D L		ankylosed		raref.	normal	—	+	(+)	ankyl.	ragged	(ankyl.)	normal	raref.	+	+	+
40 (8-3391)	38 m	3 yr.	III	D L		ankylosed		normal	normal	(+)	+	+	normal	ankyl.	(ankyl.)	normal	normal	+	+	+
41 (9- 331)	29 m	15 yr.	III	D L		ankylosed		normal	normal	—	+	+	normal	ankyl.	(ankyl.)	normal	normal	—	—	+
42 (9-1376)	30 m	15 yr.	III	D L		ankylosed		raref.	normal	(+)	(+)	(+)	ankyl.	ankyl.	narrow	normal	normal	+	+	+
43 (9-2629)	56 m	10 yr.	III	C D L		ankylosed		raref.	normal	(+)	+	—	ankyl.	ragged	narrow	normal	normal	—	—	+
44 (8- 149)	24* m	5 yr.	III	C		ankylosed		normal	normal	+	+	—	normal	normal	narrow	hands	normal	neck +	+	+
45 (9-1829)	26 m	1 yr.	III	D L		ankylosed		normal	normal	—	+	—	normal	ragged	narrow	knees	normal	—	—	+
46 (8-3059)	32 m	10 yr.	III	D L		ankylosed		raref.	normal	—	+	—	normal	ragged	ragged, narrow	normal	normal	+	—	+
47 (7- 771)	30 f	1 yr.	III	C D L		ankylosed		raref.	normal	—	+	—	normal	ragged	ragged	knee, ankle	raref.	+	+	+
48 (7-2705)	30 f	17 yr.	III	C D L		ankylosed		normal	normal	—	—	—	normal	ragged	ankyl.	elbows, knees, hands	normal	—	—	+
49 (7- 363)	55 f	9 yr.	III	L		ankylosed		normal	normal	—	+	—	normal	normal	ankyl.	normal	raref.	+	+	+
50 (6- 669)	60 m	15 yr.	III	C D L		ankylosed		normal	normal	+	+	+	?	ankyl.	narrow	normal	normal	—	—	+

some other patients. Chronic pulmonary lesions, recorded by early investigators,[3,22] were not observed in this series, although I observed the coexistence of lung abscess with Strümpell-Marie disease in 2 cases not included in this report. The influence of hereditary, endocrine, or metabolic factors could not be ascertained; none of the patients was a member of a "rheumatic" family. The occupation of the patients did not seem to play a part: there were 10 tradesmen, 8 artisans, 6 laborers, 5 peasants, 5 professional men, 8 housewives, and 8 persons without occupation in this series.

The patients came from various parts of the Near East which differ considerably in climate: the desert, seashore, plains, and high mountains. Hence a distinctive climatic factor can hardly account for the high incidence of Strümpell-Marie disease in this part of the world. But since the "macro-climate" may be less important than the "micro-climate" in the etiology of rheumatism,[21] one may speculate whether the custom of the Near East people to sleep on blankets or thin mattresses placed on stone floors, together with the absence of heating appliances, may induce rheumatic disease in susceptible persons. In most parts of the Near East, winter is a rainy rather than a cold season; but owing to the excessive humidity during this period the houses are damp and chilly for several months of the year. Most foreigners, therefore, find the winter harder to bear in Syria than, e.g. in New England or Canada. During winter the Oriental often puts on his overcoat when he enters a house, to take it off again when he leaves. Of course, no conclusions can be drawn from such general impressions.

V. THE ESSENTIAL LESION AND ITS DEVELOPMENT

According to the findings presented in Table II, lesions of the apophyseal joints were demonstrable in all the 50 cases (100 per cent); in 9 of these (18 per cent) no other parts of the vertebrae showed evi-

TABLE III

STRÜMPELL-MARIE DISEASE: FINDINGS RECORDED IN THE CLASSICAL PAPERS

Author	Clinical Findings						Postmortem Findings						Remarks
	Onset		Rigidity	Pain		Course	Curvature	Softening of bone	Vertebral bodies connected by ossified ligaments	Apophyseal joints ankylosed	Costovertebral joints ankylosed	Hip joints involved	
	in	at age		local	radicular								
Connor (1700)	No clinical data known						kyphosis	+	+	+	+	?	Incomplete skeleton found in church-yard
Fagge (1876)	?	30	+	−	+	?	kyphosis	+	−	+	+	+	Bronchiectases
Strümpell (1897)	back	3rd decade	+	−	−	ascending from lower back upward	straight back	No postmortem					Emphasizes absence of severe pain
Marie (1898)	knee, neck, back	about 30 yr.	+	+	±	ascending and descending	straight, kyphotic or Z-shaped	No postmortem					First paper in which the disease was defined as a clinical entity
Marie and Léri (1899)	back or small joints	about 30 yr.	+	+	+	ascending	variable	−	−	+	?	not examined	Autopsy incomplete
Léri (1905)	No clinical data recorded						kyphosis	+	−	+	+	+	First complete autopsy and anatomic definition of disease

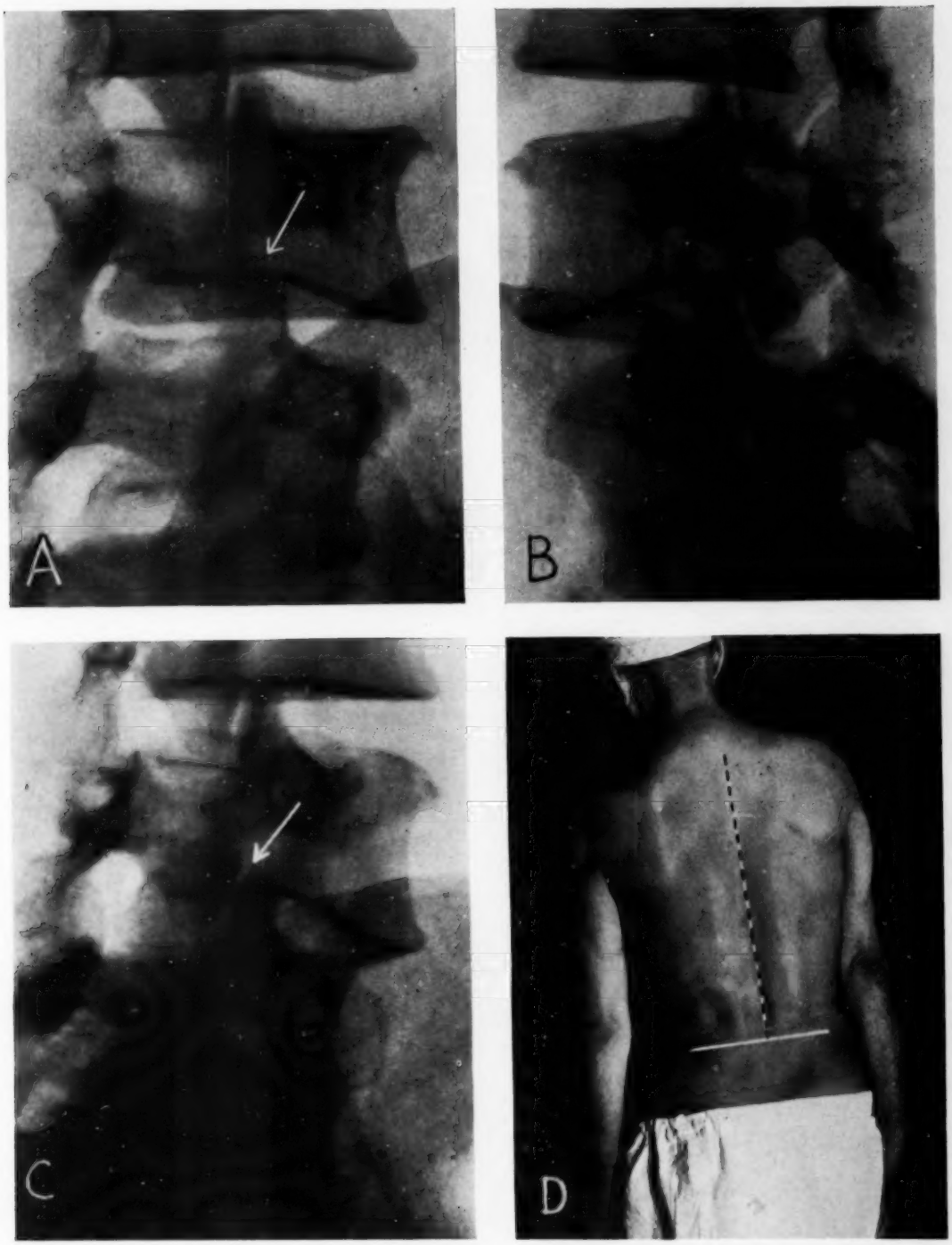

Fig. 3. Case 5. Stage 1. *A*, severe rarefaction of the articular processes of the left 5th lumbar apophyseal joint; joint space invisible owing to the dissolution of the bony outlines (arrow). *B*, normal right side for comparison. *C*, seven weeks later, one month after termination of roentgen therapy, the involved joint has resumed normal appearances (arrow). *D*, maximum amount of sidewards flexion of which the patient was capable at the time when roentgenograms *A* and *B* were taken. Slight lateral bending of the body was achieved by means of lifting of the pelvis on the convex side (horizontal line), but the spine itself was immovable (vertical line). The patient was bedfast owing to incapacitating pain in lower back. Complete recovery occurred within three weeks after beginning of roentgen therapy. The patient has been free of symptoms for over two years since.

TABLE IV

SERIAL ROENTGEN EXAMINATIONS

Case	Date	Observations
1	Feb. 19, 1936	Lumbar articular processes rarefied; lumbar facets scalloped, with narrowed joint spaces. Lig. flav. and longit. lig. at L IV/V ossified. Lumbar vertebral bodies rarefied. Sacroiliacs ragged. Discs normal. Cervical and thoracic regions not examined.
	Dec. 1, 1937	All lumbar apophyseal joints now ankylosed. Lig. flav. and long. lig. now ossified from L I to L V. Sacroiliacs in beginning ankylosis. The thoracic vertebrae show the same changes that were previously present in the lumbar vertebrae. Cervical spine normal.
	Feb. 3, 1938	Lumbar spine unchanged. Thoracic apophyseal joints now ankylosed; with ossification of the thoracic longit. lig. and lig. flava. Cervical apophyseal joint spaces slightly narrowed, with beginning ossification of long. lig.
	Aug. 7, 1940	Practically unchanged.
2	Nov. 22, 1938	Lumbar and thoracic apophyseal joints ankylosed, with rarefied articular processes, and rarefied vertebral bodies. Cervical spine normal. Sacroiliacs ragged. No ossification of ligaments.
	May 1, 1939	Entirely unchanged.
3	May 6, 1937	Lumbar articular processes rarefied, with ragged facets and narrow joint spaces. Thoracic apophyseal joints ankylosed. Cervical spine normal. Lumbar and thoracic vertebral bodies rarefied. Lumbar lig. flava ossified; thoracic longit. lig. ossified at D XI–XII. All other ligaments normal. Sacroiliacs ragged.
	May 27, 1939	Lumbar apophyseal joints now ankylosed. Lumbar long. lig. ossified. Sacroiliacs ankylosed. Otherwise unchanged.
4	Apr. 2, 1939	The 2nd lumbar and the 5th cervical apophyseal joints have rarefied articular processes, narrow joint spaces, and blurred outlines. Spine otherwise normal. Sacroiliacs normal.
	May 19, 1939	(After roentgen therapy.) Unchanged.
	Apr. 10, 1940	Unchanged.
5	June 6, 1934	The cervical, thoracic, and lumbar apophyseal joints have rarefied articular processes, narrow joint spaces, and ragged facets. All vertebral bodies rarefied. Ligaments normal except for slight ossification of long. lig. at the level of L II–III. Sacroiliac, costovertebral, and hip joints have narrowed spaces and blurred outlines.
	Dec. 10, 1936	The thoracic apophyseal joints are now ankylosed. The appearances of the cervical and lumbar apophyseal joints have not changed, except for a definite decrease of rarefaction of the articular processes. All the lig. flava are ossified. Longit. lig. unchanged. Sacroiliacs ankylosed. Costovertebral and hip joints unchanged.
	June 6, 1939	Essentially unchanged, except for increased ossification of the lig. flava. Both the vertebral bodies and the articular processes have regained normal density. Moderate increase of ossification of the lumbar longit. lig.
6	Apr. 3, 1939	Lumbar apophyseal joints have rough facets and narrow joint spaces. Thoracic and cervical segments not properly examined. Sacroiliacs normal. Ligaments normal.

Table IV—*Continued*

Case	Date	Observations
	Mar. 29, 1940	(After roentgen therapy.) Lumbar facets smoother, joint spaces apparently wider. Sacroiliacs scalloped. Thoracic apophyseal joints ankylosed, with ossification of long. lig. Hip joints involved (Fig. 9).
	Oct. 29, 1940	Beginning ankylosis of hip joints. Complete ankylosis of sacroiliacs. Otherwise unchanged.
7	Feb. 6, 1940	The cervical and lumbar apophyseal joints have rarefied articular processes, narrow joint spaces, and rough facets. Vertebral bodies and ligaments normal. Sacroiliac and hip joints have scalloped outlines. Thoracic spine normal.
	Apr. 4, 1940	The lumbar facets have become eburnated. Otherwise no change.
	Feb. 27, 1941	The cervical apophyseal joints are now ankylosed, and the cervical lig. flava and long. lig. are ossified. Otherwise no change.
8	Dec. 18, 1939	The 4th lumbar apophyseal joint only is involved: its articular processes are so strongly rarefied as to be almost indistinguishable, and the joint space is covered by a hazy shadow (Fig. 3).
	Feb. 2, 1940	(After roentgen therapy.) The involved 4th lumbar apophyseal joint is now normal.
	Apr. 6, 1940	Unchanged. Nothing pathological.
	Feb. 27, 1941	Unchanged. Nothing pathological.
9	Nov. 6, 1939	Lumbar and thoracic apophyseal joints ankylosed. Lumbar vertebral bodies moderately rarefied. Thoracic lig. flava and long. lig. ossified; the other ligaments normal. Sacroiliacs ankylosed.
	Feb. 23, 1940	The lumbar vertebral bodies have regained normal density. Otherwise no change.
10	Dec. 29, 1939	The 2nd lumbar apophyseal joint has ragged facets and a narrow joint space. The sacroiliac articular surfaces are eburnated and scalloped. Ligaments normal.
	Mar. 11, 1940	The ragged facets of the 2nd lumbar apophyseal joint have become eburnated. Otherwise no change.
11	June 23, 1939	All the apophyseal joints have narrowed joint spaces; the lumbar apophyseal joints have rough facets. The lumbar and cervical lig. flava are ossified. Sacroiliacs almost ankylosed. Hip joints blurred.
	Feb. 19, 1941	The thoracic and cervical apophyseal joints are almost ankylosed. The lumbar facets have become eburnated. The long. lig. and all the lig. flava are now ossified. Sacroiliacs and hip joints unchanged.
12	May 18, 1936	Arthritis of both hands. The 2nd and 3rd cervical apophyseal joints have ragged facets and narrow joint spaces. Spine otherwise normal. Hip and sacroiliac joints normal.
	Apr. 2, 1939	Ankylosis of 2nd, 3rd, and 4th cervical apophyseal joints, with ossification of lig. flava at this level. Otherwise no change.

Fig. 4. Case 4. Stage I. Rarefaction of 4th lumbar articular processes (black arrow), outlines of joint space blurred (white arrows). Compare with normal subjacent joint. The superjacent joint shows slight roughening of the articular surfaces (facets), corresponding to an early phase of Stage II.

dence of disease. Hence involvement of the apophyseal joints is considered here the essential lesion associated with the type of rigidity under discussion.

This observation is not new. In the classical papers ankylosis of the apophyseal joints was recorded in all the cases of vertebral stiffness in which autopsy was made (Table III); but the finding was not regarded as significant.[2,3,12,14] Soon after Marie's first and Strümpell's second article had been published, Sivén[25] and Fraenkel[5] reported arthritis of the apophyseal joints as the main lesion in cases of rhizomelic spondylosis. The presence of some more salient anatomic change, such as softening of bone or ossification of ligaments, together with the peculiar localization in spine and hips, seems to have led most other workers to discount the constant but less spectacular lesion of the apophyseal joints. Since the alterations in other vertebral parts are neither constant nor, if present, always of the same kind, interpretations became conflicting. Present concepts, including Lawford Knaggs' accepted view,[9,20] are still based upon the theories which were offered by early investigators on account of only two postmortem records.[3,15]

The data classified in Tables II and IV suggest that there are three fairly distinct stages in the development of the lesion.

Stage I. Early phase. The main sign is stippled or diffuse rarefaction of articular processes, ranging from slight loss of the

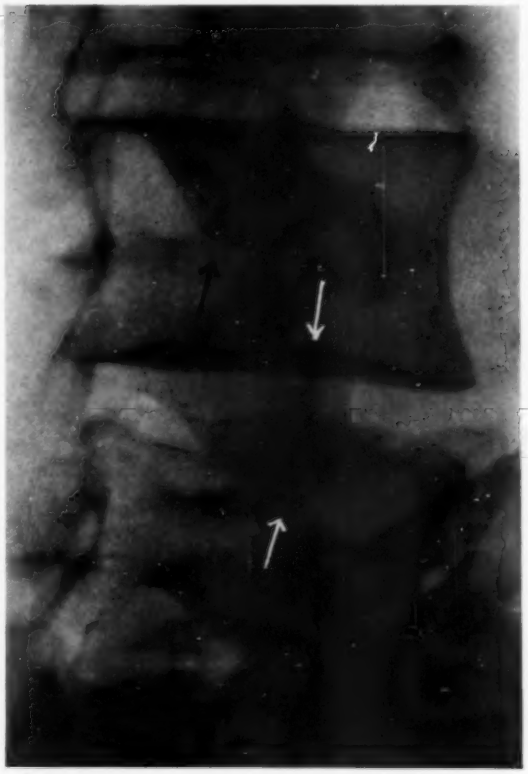

Fig. 5. Case 14. Stage II. Rarefaction of articular processes with severe narrowing of the joint space in the 4th lumbar apophyseal articulation (white arrows). Narrowing of the joint space with ragged and condensed facets in the superjacent joint (black arrows). The findings show that the appearances may vary from joint to joint even in the same vertebral section, hypertrophic reactions being sometimes superadded to an originally atrophic arthritis.

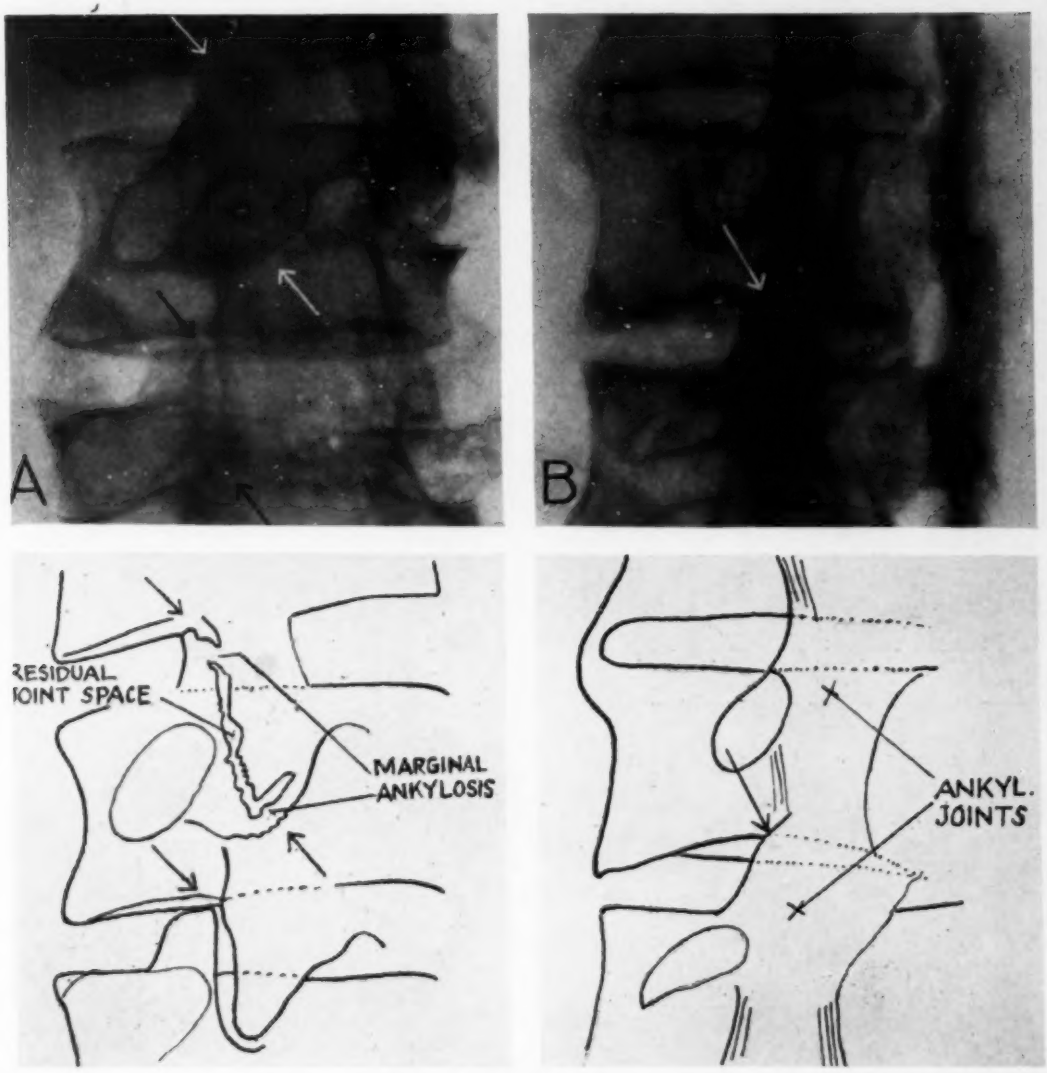

Fig. 6. Difference between circling and complete ankylosis. *A*, circling ankylosis of 3rd lumbar apophyseal joint (white arrows): the joint space is still preserved in its central parts, bony bridging being confined to the marginal regions. Compare with normal subjacent joint (black arrows). *B*, complete bony ankylosis (arrow). See the text.

density to almost complete dissolution of the structure of the bone. The facets of the involved articular processes have indistinct outlines. The intervening joint space is slightly narrowed and sometimes clouded. There is no rarefaction of the vertebral bodies, and no ossification of ligaments. In one case (Fig. 3) the involved parts resumed normal appearances after treatment, and the clinical symptoms subsided completely. This seems to indicate that the morbid reaction is reversible at this stage.

Stage II. Moderately advanced phase. The main sign is erosion, roughness, or scalloping of the facets, and definite narrowing of the joint space between them. Often, but not always, the corresponding articular processes are increased in density and the vertebral bodies rarefied. This contrasting coexistence of rarefaction in one part with increased bone density in another part of the same vertebra is almost characteristic of Stage II. Small osteophytes are sometimes present at the edges of the

facets. At the level of the involved segments slight or incomplete ossification of the ligaments may be visible. Although occasionally some of these changes become less definite after treatment (Fig. 9), there is no conclusive evidence to show that the condition is still reversible at Stage II. But the appearances may remain unchanged for many years, showing that the lesion may become arrested at Stage II at least for a long period. In other cases the disease progresses more or less rapidly towards Stage III.

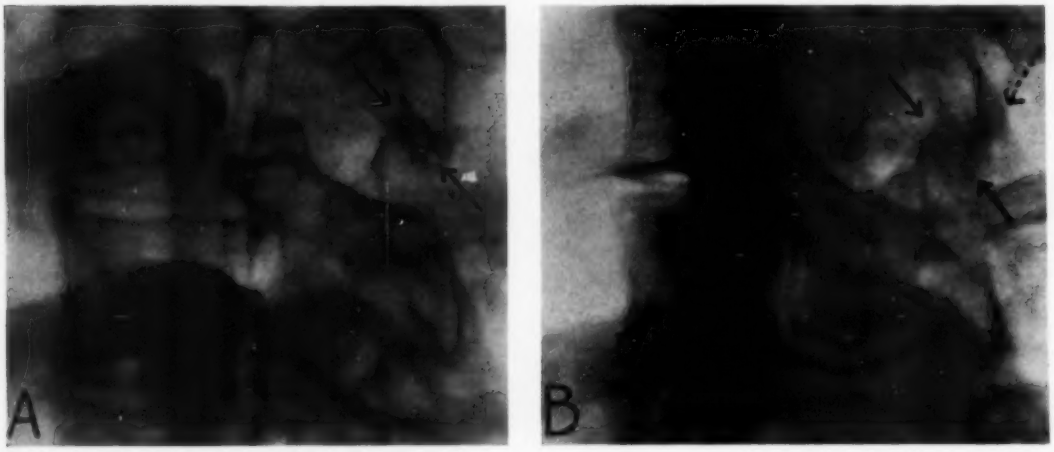

FIG. 7. Case 45. Stage III. Thoracic spine. Development of ankylosis. *A*, joint space clearly outlined, facets and articular processes normal (arrows). *B*, seven months later, the same joint is ankylosed, the joint space being filled with bony substance (arrows). The ligamentum flavum has become ossified (dotted arrow).

Stage III. Terminal phase. The main sign is ankylosis of the apophyseal joints by means of bony union: either complete, with fusion of contiguous facets and disappearance of the intervening joint space; or marginal, whereby the central part of the joint space remains radiolucent and the bony connection extends along the external or capsular region of the joint (Fig. 6, *A* and *B*). When it occurs in peripheral joints, this marginal ankylosis is sometimes named *ankylose cerclée* (circling ankylosis) in French publications.[13] Rarefaction of vertebral bodies, if present, is usually less definite than at Stage II; in fact, vertebral bodies which were found rarefied at Stage II may regain normal density at Stage III.[16] Ossification of ligaments may be absent at Stage III (Fig. 8); if present, it usually is strongly marked and extensive.

The findings also show that the lesion is confined to one or a small number of apophyseal joints at Stage I; at Stages II and III it may be either systemic or localized. Except at very late stages, when virtually all the apophyseal joints are ankylosed, the involved articulations are not all affected in the same degree: complete bony ankylosis in one joint may coexist with an incipient lesion of other joints, and several stages may be present simultaneously in the same person, and even in the same vertebral region (Fig. 4, 5 and 8).

The periods during which the lesion progresses from Stage I to Stage II or III differ considerably from case to case (Table V). Stage III may be reached within one year; but the disease may also become arrested at Stage II for over twenty-five years. During the period extending from three to about thirty years after the onset of symptoms, the number of cases of Stage II is approximately equal to the number of cases of Stage III. This fact is of some diagnostic importance, since at Stage II the lesion is usually confined to, or most

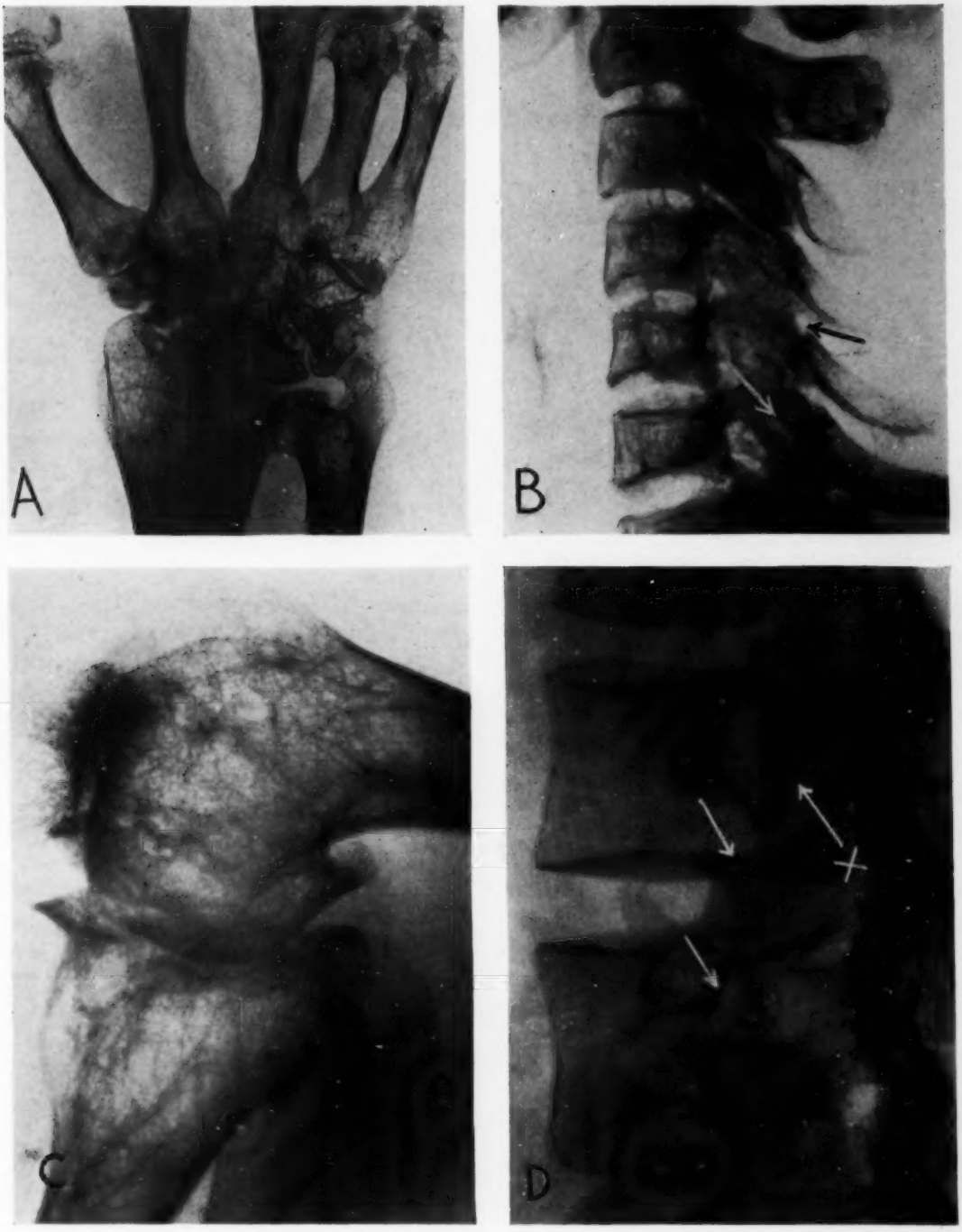

FIG. 8. Case 48. Almost all of the synovial joints of the body were involved. *A*, narrowing of joint spaces of wrist, with partial ankylosis, rarefaction of bones, but also some moderate condensation on radial side. *B*, some of the cervical apophyseal joints are ankylosed (black arrow), others show narrowed joint spaces with ragged and condensed facets (white arrow). Rarefaction of articular processes. *C*, knee ankylosed in flexed position, articular bone rarefied, but also some marginal overgrowth. *D*, the 4th and 5th lumbar apophyseal joints are ankylosed (arrows), while the 3rd has a very narrow joint space with ragged and condensed facets (arrow at ×). Lesion strictly confined to the apophyseal joints; the vertebral bodies, discs and ligaments are not involved. Clinically, a typical instance of Strümpell-Marie disease. Note that the lesions of the apophyseal joints are identical in type with those of the peripheral articulations.

TABLE V

RELATION BETWEEN STAGES AND DURATION OF SYMPTOMS

	Less than 1 yr.	1–2 yr.	3–4 yr.	5–6 yr.	7–8 yr.	9–10 yr.	11–12 yr.	13–14 yr.	15–16 yr.	17–18 yr.	19–20 yr.	Over 20 yr.	Total Number of Cases
Stage I	4	1											5
Stage II	1	5	3	5	3	4	1	1				1	24
Stage III	1	3	5	3		4		3	1			1	21

definite in, the apophyseal joints. Ossification of ligaments, which is often considered a diagnostic criterion, is not conspicuous at Stage II, if present at all. Since a lesion of the apophyseal joints is not always demonstrable by the conventional roentgenographic technique,[6,16] a number of cases may have escaped recognition, or may have been grouped with "entities" to which they do not belong in reality. I recovered among my own records 8 such cases which I had previously labelled fibrositis, vertebral rarefaction, or obscure rheumatic disease.

VI. ACCOMPANYING LESIONS OF THE VERTEBRAE AND PELVIS

A. Rarefaction of Vertebral Bodies. This is distinct from the rarefaction which is confined to the articular processes during Stage I. The vertebral bodies were found to be rarefied in 26 cases (52 per cent). This rarefaction was absent in all the cases of Stage I, but present in 75 per cent of the cases of Stage II and in 25 per cent of the cases of Stage III. This decreasing frequency of rarefaction at Stage III is in accord with the observation showing that the vertebral bodies tend to regain normal density when bony ankylosis of the apophyseal joints has taken place.[16] For example, in Case 26, Table II (No. 5 of Table IV), the vertebral bodies were strongly rarefied in June, 1934; but their density was normal again in December, 1936, and was still normal in June, 1939, when ankylosis of the apophyseal joints was found to be complete.

These observations show that rarefaction of vertebral bodies, being neither a constant nor an early sign of Strümpell-Marie disease, cannot be considered pathognomonic.

B. Ossification of vertebral ligaments, which is easily demonstrable on roentgenograms made in the tangential projection, is not always visible in routine views.[19] Ossification of the longitudinal and interspinous ligaments was analyzed on lateral

TABLE VI

OSSIFICATION OF VERTEBRAL LIGAMENTS

	Stage I	Stage II	Stage III	Total
Flava alone	—	2	4	6
Flava and longitudinal	—	1	6	7
Flava, longitudinal and interspinous	—	3	5	8
Longitudinal alone	—	5	3	8
Longitudinal and interspinous	—	2	—	2
Interspinous alone	—	—	—	0
Flava and interspinous	—	1	2	3
Total	0	14 = 58% of cases of stage II	20 = 95% of cases of stage III	34 = 68% of all cases

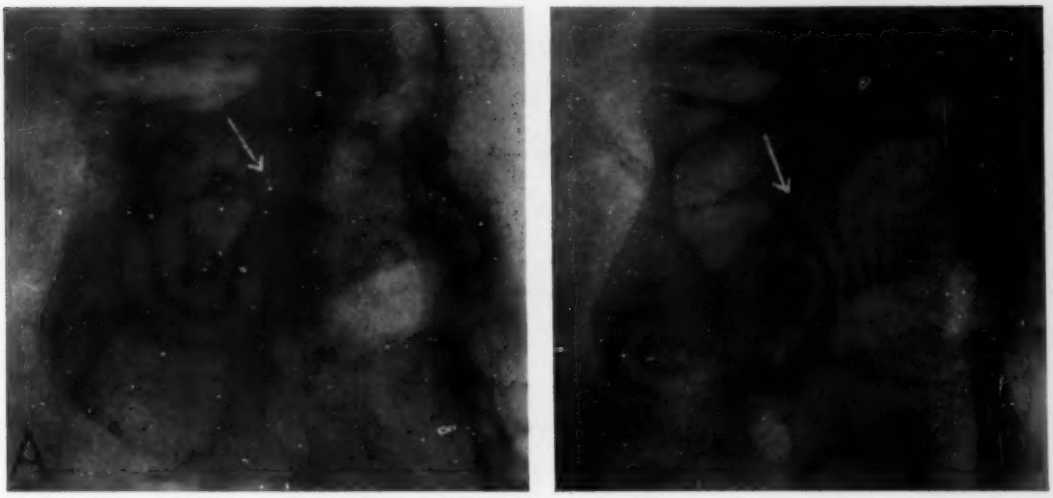

Fig. 9. Case 45. Result of roentgen therapy. Lumbosacral junction. *A*, rarefaction of superjacent articular process of 5th lumbar apophyseal joint; facets blurred; joint space almost invisible. *B*, two months later, after termination of roentgen treatment, rarefaction is no longer definite, normal bone density being regained; the joint space has become visible rather clearly. The patient, bedridden when treatment was begun, resumed his normal occupation two weeks after its termination and has remained free of symptoms for over a year since.

views; of the ligamenta flava, on oblique views; and of the lateral fibers of the anterior longitudinal ligament, on anteroposterior views. Table VI shows that ossification was present in none of the cases of Stage I, in one-half of the cases of Stage II, and in a majority of cases of Stage III. The ligaments close to the neural arch and apophyseal joints were found to be ossified more frequently and more markedly than those of the more ventral parts. The correlation between the degree of ossification and the three stages of the apophyseal lesion was analyzed on roentgenograms of the anterior longitudinal ligaments which can be studied more accurately than the less accessible ligaments of the posterior parts of the spine. In Table VII, "grade A" implies the presence of small thorn-like ossifications at the edges of the vertebral bodies, resembling osteophytes but for their smaller size and lesser density. "Grade B" means additional patchy and incomplete ossification extending further across the intervertebral space. "Grade C" signifies complete bridging of this space. No ossification was present at Stage I; there was a fairly uniform distribution of the three grades at Stage II; and grade C was predominant at Stage III. It should be noted

Table VII

OSSIFICATION OF LONGITUDINAL LIGAMENTS

	Stage I	Stage II	Stage III	Total
Grade A	—	3	—	3
Grade B	—	5	1	6
Grade C	—	4	12	16
Total	0	12 = 50% of cases of stage II	13 = 61% of cases of stage III	25 = 50% of all all cases

that this correlation between the degree of ossification and the stages of the lesion was entirely independent of the duration of the disease. This is perhaps not surprising, as the degree of the changes in the apophyseal joints also does not depend on the time factor.

The data, in conjunction with those presented in Table IV, indicate that ossification of ligaments begins to appear when the disease is moderately advanced. Ossification of ligaments lags behind the development of the apophyseal joint lesion and is not a constant finding. This does not support the view that the clinical syndrome of Strümpell-Marie disease is caused by a systemic ossification of ligaments. In one-third of our patients of this group, no ossification could be demonstrated in the different vertebral ligaments.

TABLE VIII

INCIDENCE OF SARCROILIAC INVOLVEMENT

	Stage I	Stage II	Stage III
Grade A	3	—	—
Grade B	—	11	7
Grade C	—	12	10
Total	3 = 60%	23 = 96%	17 = 81%

C. Involvement of the sacroiliac joints, ranging from blurring of the joint outlines to complete bony ankylosis, was present in 43 instances (86 per cent). In the remaining 7 patients (14 per cent) the sacroiliac joints were normal both on clinical examination and roentgenologically; in these cases, the apophyseal joint lesion was confined to the thoracic or cervical vertebrae. In Table VIII, in which the roentgenographic findings are grouped according to their degree and in conjunction with the three stages of the disease, "grade A" implies blurring of the sacroiliac articular outlines; "grade B," scalloping of the articular surfaces with or without eburnation of the adjacent bone; "grade C," complete or almost complete bony ankylosis. The data of Table VIII show that the incidence of sacroiliac involvement increases as the lesion of the apophyseal joints evolves towards Stage III. But the severity of the sacroiliac lesion is not proportional to the severity of the apophyseal lesion. Ankylosis of the sacroiliac joints may either precede or follow ankylosis of the apophyseal joints. For example, in Case 45 (No. 6 of Table IV), the sacroiliac joints were still normal when the apophyseal joints were already completely ankylosed; but one year later the sacroiliac articular surfaces became ragged, and this appearance did not change during the subsequent six months.

Since great diagnostic importance is usually given to the sacroiliac lesion, the following inferences from the above findings may have some significance: (1) the sacroiliac joints are not involved in every case, especially not when the disease begins in, or remains confined to, the cervical or thoracic segments; (2) even when the lumbar and lumbosacral apophyseal joints are involved, the sacroiliac joints may remain normal for periods of years. An early diagnosis cannot be based, therefore, upon the presence or absence of sacroiliac lesions. Their presence merely supports the diagnosis of Strümpell-Marie disease, but their absence does not disprove it.

D. Involvement of the Costovertebral Joints. Diminished respiratory expansion of the chest, suggestive of involvement of the costovertebral joints, was noted in 31 cases (62 per cent), all of them at Stages II and III. In 15 of these patients, roentgenograms showed roughening, eburnation, or ankylosis of these articulations. Owing to the great technical difficulties encountered in obtaining adequate roentgenograms of these joints, the data could not be analyzed further.

E. Involvement of the vertebral symphyses, shown by alterations of the intervertebral spaces and horizontal vertebral surfaces, was not demonstrable in this series of cases. It is true that fragmentation of the vertebral disc cannot be shown on roentgeno-

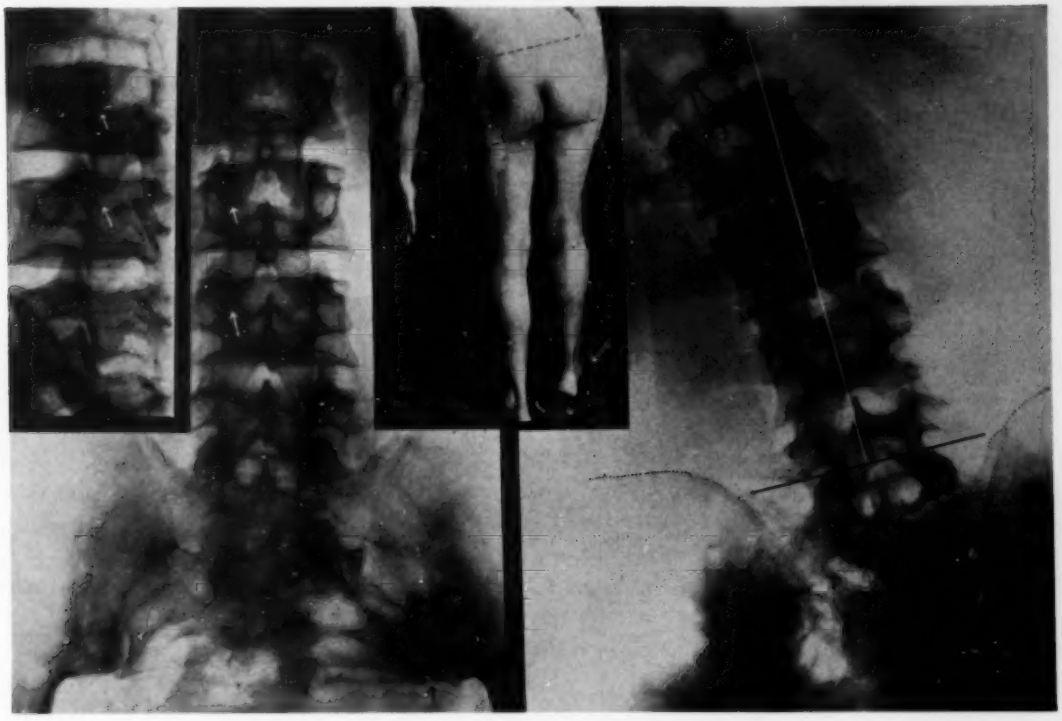

Fig. 10. Case 2. Stage 1. The left 3rd and 4th lumbar apophyseal joints have blurred facets and narrow joint spaces (white arrows on insert left); the sacroiliac joints are involved (black arrow). Insert in center shows maximum amount of sidewards bending of which the patient is capable: most of this motion is achieved by means of lifting of the pelvis and foot (arrow) on the side of the convexity. The patient was not conscious of making these auxiliary movements. Roentgenogram taken during sidewards bending (upright position, 4 ft.) reveals slight flexion of upper lumbar spine; the movement of the pelvis is indicated by the black line drawn parallel to the upper horizontal surface of the 1st sacral vertebra; the 3rd, 4th, and 5th lumbar segments are almost completely rigid.

grams at early stages; but it leads to narrowing of the corresponding interspace within less than one year in most cases, and slight irregularities or eburnation of the vertebral surfaces become visible not much later, as a rule. The absence of such changes in patients whose vertebral symptoms had persisted for ten years or more virtually excludes a lesion of vertebral symphyses in these cases. In 2 patients with Strümpell-Marie disease not included in this report, several intervertebral spaces were found to be narrowed in segments distant from the vertebrae involved by apophyseal joint lesions; this was interpreted as an accidental coexistence of two distinct lesions.

F. Involvement of the Pubic Symphysis. I have observed complete ossification of the pubic symphysis in 2 or 3 cases of Strümpell-Marie disease not recorded here; but in the present series, the pubic symphyses appeared to be normal. In one case, the symphysis seemed to be bridged by what appeared to be an ossified ligament.

In 3 cases irregular bony spikes, suggestive of ossification of muscles or tendons, projected from the inferior margins of the pubic and ischial bones. Rarefaction of the pubic bones was noted in 7 cases (14 per cent) in the simultaneous presence of rarefaction of vertebral bodies.

VII. Involvement of Other Joints

Limitation of movements and pain in one shoulder or both was a common symptom (42 cases: 84 per cent). The roentgen findings were negative except for 2 cases with complete ankylosis of almost all the

joints of the body. I found it difficult to ascertain whether the symptoms were caused by arthritis, muscle spasm, or radicular neuritis.

In 24 cases, pain and limited mobility were present in the hip joints (48 per cent); in 16 of these, roentgenograms disclosed lesions of these joints ranging from blurring of the articular outlines to almost complete ankylosis.

Peripheral joints—fingers, toes, wrists, ankles, elbows, or knees—were found to be involved both clinically and roentgenologically in 9 instances (18 per cent). In 4 other patients there was pain, sometimes with some swelling, in peripheral joints in the absence of definite evidence of arthritis. These patients had signs of radicular neuritis, and the articular symptoms may have been due to radicular manifestations, since early stages of neurotrophic lesions cannot always be distinguished from arthritis.[18]

VIII. COMMENTS

The roentgen analysis of the lesions under discussion involves many sources of error. There is, first, the fundamental limitation in the roentgenologic interpretation of arthritis: the key structures, cartilage and synovial membrane, cannot be seen on roentgenograms except by the use of auxiliary methods which are impracticable in the inaccessible apophyseal joints. Lesions of cartilage and synovial membranes are recognized by inference rather than by direct evidence, e.g., from the width of the joint space, or from erosion of the bony articular surfaces. Second, technical factors add to this basic difficulty. The curved planes of the facets may overlap, especially in the lumbar spine, thereby obscuring the joint space. In the thoracic segments adjacent bones often overshadow the articular processes. Like other compact bones, the articular processes do not easily undergo rarefaction; and rarefaction may not always become visible on roentgenograms. Variations of density in the articular processes are difficult to evaluate; differences in size, position, and amount of cortical bone often cause normal articular processes of the same vertebra to be of different density. Densitometry is not applicable, as the density of intervening viscera and of their contents is subject to excessive variations; and superimposition of intestinal gas upon a lumbar articular process, or of a bronchial lumen upon a thoracic facet, may produce appearances falsely indicative of rarefaction. On roentgenograms, thickening of the joint capsule, which is easily demonstrable for the peripheral joints, is visible only exceptionally in the apophyseal joints.[16] Finally, since early and active stages of arthritis are not often accessible to anatomic study, the roentgen interpretation of these lesions is not yet based on firm ground.

For all these reasons the results of roentgen studies of the apophyseal joints must be considered with reserve. The roentgenologic method is imperfect. But the anatomical method also has its limitations. The condition seen at autopsy of many vertebral lesions is essentially a scar. The morbid process which produced the scar cannot be recognized directly, but only by inference and analogy. Consequently, direct observation of the development of a vertebral lesion had to be attempted, even though with the method used the results could not be complete. Together with the complete but indirect anatomical evidence, the incomplete but direct roentgenologic evidence has its value. This is pointed out here because the inferences drawn from roentgen examinations made during life do not always tally with the conceptions reached by the purely anatomical approach.

IX. CLINICAL FINDINGS

Laboratory findings in this series are not sufficiently complete to allow statistical analysis. The results of physical examinations are grouped in Table IX and Figure 11 with the three stages and with the condition of the apophyseal joints, vertebral bodies, and ligaments.

There were three main clinical manifestations in this series: (1) stiffness of the

back and/or neck; (2) pain and/or tenderness of the back and/or neck; (3) signs or symptoms of radicular neuritis. In Table IX and Figure 11 "rigidity" means severe limitation of vertebral movements, with a range of lateral lumbar flexion not exceeding 5 degrees, other motions being restricted proportionally. "Local pain" implies spontaneous pain in the neck and/or back, usually associated with tenderness on pressure upon the spine about 1 inch to the left or right of the spinous processes. "Radiculitis" or "radicular manifestations" signifies frank radicular neuritis; pain radiating to the flanks or limbs in other than segmental distribution was not included, although it may be due to involvement of nerve roots in certain cases, since slight or incipient radicular neuritis cannot always be distinguished from referred pain.[17,18]

The tabulated findings show that rigidity was associated with lesions of the apophyseal joints in 100 per cent of the cases, regardless of the severity and extent of these lesions: patients with an incipient or slight lesion confined to one single apophyseal joint were found to be as stiff as patients

TABLE IX

RELATION BETWEEN LESIONS AND SYMPTOMS

	Apophyseal Joints Involved in the Absence of		
	Rarefaction of vertebral bodies	Ossified ligaments	Both rarefaction and ossification
Local pain	15 = 62.5%	16 = 95%	7 = 87.5%
Radicular symptoms	4 = 16.6%	5 = 29%	3 = 37.6%
Rigidity	24 = 100%	17 = 100%	8 = 100%

with bony ankylosis of most of the apophyseal joints (Fig. 3). This rigidity was present in the absence of rarefaction of vertebral bodies, of ossification of ligaments, and of other changes not involving the apophyseal joints. It has been shown that extensive ossification of vertebral ligaments need not interfere with normal vertebral movements.[19] Although in biologic sciences a correlation of 100 per cent, which means a correlation coefficient of 1.0, is rightly considered to be too good to be true, the above findings seem to prove that the

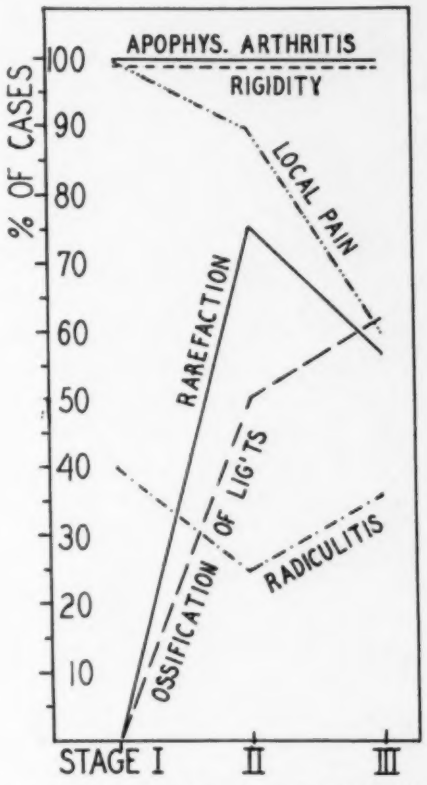

FIG. 11. Graph showing the clinical findings observed during the three stages, and the correlation of the apophyseal joint lesion with both rarefaction and ossification of ligaments. See the text.

stiffness of back or neck present in Strümpell-Marie disease is a direct and constant result of the apophyseal joint lesion under discussion.

Local pain, a constant symptom at Stage I, was less frequent at Stage II, and again less common at Stage III. This is in accord with the classical descriptions which mention that pain subsides as the disease progresses. Local pain was independent of the condition of the vertebral bodies and ligaments in our series; like rigidity, it seemed to be caused by the lesion of the apophyseal joints alone.

Radicular neuritis was noted in about

one-third of all cases; its incidence was highest at Stage II and lowest at Stage III.

In Table X the clinical manifestations are grouped in conjunction with the roentgenologic appearances of the apophyseal joints, considered according to the condition of the articular processes, their facets, and joint spaces. Rigidity was present whenever one of these parts was involved. Local pain was constant in the presence of rarefied articular processes and/or of eroded facets, but comparatively rare in the presence of ankylosis. The incidence of radicular manifestations was highest in the presence of ankylosis. This analysis does not add much to the results obtained from the data of Table IX.

TABLE X

RELATION BETWEEN LESIONS AND SYMPTOMS

	Local Pain	Radicular Manifestations	Rigidity
Articular processes rarefied	22 = 100%	6 = 27%	22 = 100%
Facets ragged	24 = 100%	5 = 20.8%	24 = 100%
Apophyseal joints ankylosed	14 = 70%	8 = 38%	21 = 100%

Persistent contraction of muscles was noted in many patients, but was not tabulated since I did not know of an objective diagnostic test. On palpation, the muscles involved, usually the hamstring group and the stretchers of the lower back, gave the impression of being thinner, harder, and less pliable than normal. In 47 patients (94 per cent) of both sexes, of different ages, and at different stages of the disease, a striking loss of the activity of the facial muscles was observed. This produced an inert or vacant expression which contrasted strongly with the lively facial activity commonly exhibited by Near East people. The absence of this play of expressions in our patients was therefore more conspicuous perhaps than in instances observed in other countries where persons are more reluctant to show their feelings. Except for a casual reference made by Marie in his first paper, this rigidity of the face has not been recorded in the publications available to me. One may speculate whether it is due to a reflex inhibition, a part of the general attempt to avoid bodily movements since these elicit pain; or whether it is caused by a systemic disease of the musculature There seems to be no method by which this question could be investigated at present.

XI. THE PROBLEM OF THE STIFF BACK

The questions relating to normal and limited mobility of the back and neck are complex and have many side issues; it is not possible here to discuss them at length. Some of the aspects of the problem are presented separately. In connection with the subject under review, three points are of interest: (1) the movements of the back and neck in the presence of lesions of the vertebral symphyses; (2) the movements of the back and neck in the presence of lesions of the apophyseal joints; (3) stiffness of the back or neck caused by lesions other than vertebral.

(1) Of 50 patients with thinned intervertebral discs, with or without osteophytes at the vertebral edges, but *with normal apophyseal joints*, 48 (96 per cent) were not conscious of a limitation of the involved spinal area, nor did physical examination reveal limited movements. Photographs sometimes disclosed a moderate flattening of the spinal curves during sidewards flexion. Measurements made on roentgenograms showed normal ranges of motion in 39 cases (78 per cent); a slight limitation, in 8 patients (16 per cent); and definite limitation, in the remaining 3 patients (6 per cent). When present, limitation of movements was confined to the segments with thinned discs, adjacent segments showing either normal or moderately increased mobility. Consequently, the *total* movement intended could be achieved by means of increased mobility of the neighboring vertebrae. This seems to account for the fact that the patients were not conscious of

a limitation of the movements of the involved pairs of vertebrae. These results confirm findings previously reported.[16,18,19]

(2) Of 20 patients with lesions suggestive of hypertrophic (osteo-) arthritis of the apophyseal joints, such as eburnation of the facets, moderate narrowing of the joint space, osteophytes at the articular margins, 14 (70 per cent) complained of moderate stiffness in the involved region, and mobility was found to be diminished on roentgenographic records. In patients with findings indicative of rheumatoid arthritis of the apophyseal joints, as shown by rarefied articular processes, blurred facets, and narrowed joint spaces, we noted stiffness of the involved vertebral region, usually associated with severe pain, in 28 out of 30 cases (93 per cent). In contrast to the patients with lesions of the vertebral symphyses, the movements of the vertebrae involved and of at least one superjacent pair of vertebrae were found to be definitely limited on roentgenograms. In most of these cases, physical examination revealed stiffness of the entire spinal section in which the apophyseal arthritis was localized, regardless of the number of apophyseal joints involved. For example, atrophic arthritis of a single lumbar apophyseal joint caused the whole lumbar spine to be immovable both actively and passively (Fig. 3).

(3) Limitation of vertebral movements was observed to occur in the presence of renal calculi, paranephric abscess, gallbladder disease, furuncles of the neck or back, in the absence of demonstrable vertebral abnormalities. Usually, flexion was free towards the side of the diseased viscus, but limited towards the opposite side. Only 5 out of 28 patients of this group were conscious of the limitation of motion. In persons suffering from "lumbago," active movements were strongly restricted, but almost the full range of motion could usually be achieved by gentle passive bending and extending.

This brief summary of observations on vertebral movements may be sufficient to show that limitation of the movements of back and neck, as experienced by the patient and demonstrable on roentgenograms, is almost constantly present when the apophyseal joints are involved, but is either slight, unnoticed, or absent when only the vertebral symphyses are diseased.

XII. THE PROBLEM OF PAIN OF VERTEBRAL ORIGIN

In recent years, pain in the lower back has been ascribed to a variety of abnormalities in the lumbar and lumbosacral vertebrae. In a series of 100 cases of backache, different lesions and abnormalities of the lumbar vertebrae were noted in 82 instances. A control series of 100 cases showed, however, that similar lesions and abnormalities were present in 61 persons in the absence of symptoms. It is difficult to understand why the same lesion should cause symptoms in one case, but be unnoticed by other patients. Age, habits, posture, muscular coordination, and mental factors are perhaps responsible for the discrepancy; and reflex pain due to some unrecognized lesion of pelvic or abdominal viscera may come into play.

These limitations do not apply in the same measure to the question of pain in the neck. Static and postural factors play a less important part, reflex pain is relatively rare, and mental influences do not seem to affect the neck as commonly as the lower back. Hence the problem of vertebral pain was studied on patients with lesions of the cervical vertebrae. Of 19 patients with lesions of the cervical apophyseal joints, 18 complained of constant or recurrent pain in the neck; but only 3 out of 60 patients with lesions confined to the vertebral symphyses felt pain in the cervical region.

Segmental neuritis is caused by lesions of the vertebral symphyses in a large number of cases.[17,18] In a series of 100 instances of flattening of cervical intervertebral discs, symptoms of radicular neuritis were noted in 82 persons; only 2 of these complained of pain in the neck; the others were not conscious of any discomfort localized in the

neck. Lesions of the apophyseal joints, while causing pain in the neck in most instances, do not seem to induce radicular neuritis in many cases: in only 6 out of 19 patients with lesions of the cervical apophyseal joints were symptoms of segmental neuritis noted. I have been quoted erroneously as having stated that arthritis of the apophyseal joints (spondylarthritis) is the most common cause of radicular neuritis of vertebral origin; but I have pointed out[16,19] that compression of the nerve root depends on the spatial relations between the caliber of the root, the original width of the neural foramen, and the amount of constriction of the foramen. In segments in which the nerve is slender and the foramen wide, such as the thoracic spine, narrowing of the foramen need not cause the roots to be encroached on; but where the nerve is thick and the foramen relatively narrow, as in the cervical region, a slight constriction of the foramen is often sufficient to produce pressure upon the root. In general, the amount of narrowing of the foramen that is caused by flattening of the corresponding disc is definitely greater than the constriction caused by lesions of the apophyseal joint. This, together with the greater incidence of lesions of the discs, makes flattening of the discs the most common cause of radicular neuritis, although, according to the foregoing discussion, compression of nerve roots may occur in many other vertebral diseases.

The observations seem to show that pain in the neck is a common symptom of lesions of the cervical apophyseal joints, but rare in the presence of lesions of the cervical vertebral symphyses. On the other hand, radicular neuritis is more frequently caused by lesions of the discs than by lesions of the apophyseal joints.

XIV. DISCUSSION

The roentgen findings above recorded indicate that the lesion which is associated with the clinical manifestations of Strümpell-Marie disease is localized in the apophyseal joints. Rarefaction of articular processes with narrowing of the intervening space is present at incipient and early stages. The lesion may then evolve rapidly towards complete or circling bony ankylosis; or it may take a slower course and become arrested at intervals, during which the articular surfaces may become rough and eburnated. Ankylosis in one joint may coexist with eburnation in another joint, or the two may occur simultaneously in different parts of the same joint. This would seem to indicate that the two morphologic characters, viz., ankylosis and eburnation, correspond merely to different phases of the same morbid condition.

These appearances, and the sequence of events, are typical of rheumatoid (atrophic) arthritis. Rheumatoid arthritis is potentially always an ankylosing lesion. But marginal osteophytes and eburnation, which are usually considered characteristic of osteoarthritis (hypertrophic arthritis, degenerative joint disease), may occur at quiescent or arrested stages of rheumatoid arthritis of peripheral joints. The anatomic appearances are then ambiguous even histologically.[10] The data above recorded show that, as in other joints, rheumatoid arthritis of the apophyseal joints need not cause ankylosis in every case. I have previously adopted Fraenkel's term, ankylopoietic spondylarthritis, to designate the lesion under review. But since ankylosis is only the potential result of rheumatoid arthritis, and since the observations show that the ankylosing is actually continuous with the rheumatoid form, I now believe that a distinction between ankylopoietic and rheumatoid spondylarthritis can no longer be made.

In the presence of rheumatoid arthritis of peripheral joints, the adjacent bone may become rarefied. The amount of rarefaction is usually proportional to the activity and duration of the articular lesion. The rarefaction of vertebral bodies which is present at moderately advanced stages of atrophic spondylarthritis would seem to correspond to this para-articular rarefaction of other bones. Hyperemia[13] and proliferation of

granulation tissue[20] are held to account for this rarefaction. Owing to their cancellous structure and their abundant venous sinuses,[27] the vertebral bodies undergo rarefaction readily. It is believed[13] that the lime salts set free by rarefaction can be deposited in adjacent connective tissue if this has become de-differentiated as a result of the complex reactions which are usually called inflammation. Callus, for instance, is formed in this manner at least in many cases. The ligaments of the spine, which are the only connective tissue close to the vertebrae, may take part in the inflammation of the apophyseal joints and may then become ossified when neighboring bone is rarefied and mobility is limited.[19] This view is supported by the finding of a predominance of ossification in the ligaments which surround the apophyseal joints. Further research into the general pathology of connective tissue may alter or amplify this theory; but the fact remains that rarefaction of vertebral bodies and ossification of vertebral ligaments are neither constant nor primary lesions, and that the clinical manifestations of Strümpell-Marie disease cannot be ascribed to either of them. Table XI sums up our observations in an attempt to incorporate the various concepts of the pathology of this disease into the more general view obtained from the findings above recorded.

TABLE XI

SYNOPSIS OF FINDINGS

	Apophyseal Joints	Vertebral Bodies	Vertebral Ligaments	Involvement of Other Joints	Pain		Rigidity	Designations and Synonyms
					Local	Radicular		
Stage I	articular processes rarefied; joint space narrowed	normal	normal	variable	++	±	+	atrophic spondylarthritis
Stage II	joint space narrowed; facets ragged, sometimes eburnated	often rarefied	often in beginning ossification	variable	±	±	+	atrophic spondylarthritis, sometimes with secondary hypertrophic reactions
Stage III	ankylosed	sometimes rarefied, but normal bone density may be regained	often ossified	variable	∓	±	+	if hips and shoulders involved: rhizomelic spondylosis or Strümpell-Marie disease; ankylosing spondylitis if ligaments ossified: spondylitis ossificans ligamentosa if rarefaction present: atrophic spondylitis if ankylosis of apophyseal joints complete: ankylopoietic spondylarthritis—in the German terminology: Bechterew disease

Clinically, two cardinal symptoms of rheumatoid arthritis, pain and limitation of movements, are almost constantly present when the apophyseal joints are involved. The third main sign, swelling of the joint, may also exist, but cannot be recognized because of the inaccessible position of the apophyseal joints. Its presence may be inferred from symptoms of radicular neuritis caused by compression of nerve roots; but, owing to the spatial relations above mentioned, swelling of the apophyseal joint capsule need not produce compression of nerves in every case.

Limitation of vertebral movements was

equally definite at incipient stages of apophyseal arthritis as in the presence of complete ankylosis of these joints. Control series disclosed that lesions of the vertebral symphyses, which often induce radicular neuritis, cause pain in the spine and limitation of vertebral movements only exceptionally. It has also been shown that ossification of ligaments need not interfere with normal vertebral mobility,[19] and complete rigidity of the spine was present in several patients of this series in the complete absence of ossified ligaments. Hence the findings would seem to show that in the presence of Strümpell-Marie disease, pain and rigidity are caused by the lesion of the apophyseal joints alone.

It has been demonstrated that lesions of the apophyseal joints conform to the anatomic conception of arthritis.[16] Lesions of the vertebral symphyses differ fundamentally from arthritis, since the symphyses are devoid of synovial membranes and free cartilaginous surfaces, in which arthritis, especially rheumatoid arthritis, is localized by definition. Because of the common occurrence of osteophytes, eburnation, or rarefaction, lesions of the vertebral symphyses are usually considered arthritic, but rarefaction and bony overgrowth are uncharacteristic reactions common to a great variety of bone lesions other than arthritic.

The findings in this series suggest that lesions of the apophyseal joints are distinct from lesions of the vertebral symphyses not only anatomically but also in their clinical manifestations. Lesions of the apophyseal joints are associated with pain in the spine and with limitation of vertebral movements. Lesions of the vertebral symphyses do not produce these clinical manifestations. The patient whose radicular neuritis is caused by a lesion of the vertebral symphyses usually refuses to believe that anything is wrong with his spine. The patient who suffers from an arthritis of the apophyseal joints (spondylarthritis) is in no doubt about the seat of the trouble.

XIV. THERAPY

The usual therapeutic measures, such as rest, physiotherapy, administration of gold salts, of the various sulfanilamid compounds, of vitamins, etc., failed to produce any improvement in the patients of this series. Roentgen therapy, advocated by some authors,[8] was given to 17 patients. According to measurements made on specimens, it was estimated that optimal roentgen-ray absorption at the depth of the apophyseal joints could be achieved by using the following factors: 135 to 150 kv., according to the build of the patient; 5 ma.; 0.5 mm. Cu plus 1 mm. Al filtration; target-skin distance of 10 inches (25 cm.); between 18 and 22 r per minute, according to the penetration. After many trials and failures, it was found that individual doses of 40–60 r yield the best therapeutic results. Each individual portal or field, usually 15 by 15 cm. in size, received 40–60 r once or twice at intervals of from three to seven days. A total dose of about 240 r given through four portals was usually sufficient for the treatment of the entire spinal column. This total was administered in the course of one week in most cases. The series was repeated when symptoms recurred, after intervals varying between six weeks and seventeen months.

It should be noted that the penetrations used were lower, and the doses given smaller, than those of the methods recommended by other workers or practiced in most other institutions. But an increase of kilovoltage, of the number of roentgens, or of both, failed invariably to bring about improvement in patients not previously treated, and resulted in recurrence of pain in cases in which relief had been obtained by means of the radiation technique above described. All being equal, increase of milliamperage (up to 25 ma.), while shortening the periods of treatment because of a higher r per minute output, did not produce results as favorable as those to be described presently. It would seem, then, that, in addition to adequate penetration and dos-

age, the time factor plays a definite part in this form of radiation treatment.

In order to exclude overlapping of the results of different therapeutic measures, all other types of treatment, including rest and analgesics, were discontinued several days before and throughout the period of roentgen therapy. Bedridden patients were taken out of bed as often and for as long as possible. All of the patients treated were incapacitated by pain and entirely stiff before roentgen treatment. Few of them were able to walk.

Of these 17 patients, 7 were cases of Stage III, 6 of Stage II, and 4 of Stage I. In 2 cases of Stage III, roentgen treatment did not produce any result. These patients were in poor health generally, and the whole spine was ankylosed. In the 5 other cases of Stage III pain subsided completely a few days after termination of the first series of treatments. Vertebral mobility did not increase, but the patients stated that they felt more movable, probably owing to the disappearance of pain and muscle spasm. The 6 patients of Stage II responded more dramatically. They felt free of pain almost at once and were able to resume work within a week after termination of the first series of treatments. Four of them returned for treatment at intervals of four to seventeen months because of recurrence of pain and stiffness, and experienced the same relief after these second series of treatments. Photographic records showed that vertebral movements did not actually increase although the patients themselves believed that their mobility had become almost normal. In the 4 cases of Stage I, the therapeutic results were even better. Two of these patients who were entirely incapacitated and had been bedridden for over one month prior to treatment, unable to walk without being supported by two attendants, and in continuous severe pain, began walking unaided two days after the first series of treatments was completed, and were able to resume heavy farm work two weeks later. In the 2 other patients of Stage I, the pain and disability were not equally severe, and the treatment resulted in complete relief of the symptoms. All these patients had been observed during periods of from two to fourteen months prior to the treatment, and no similar therapeutic results had been obtained by any other method. The results of roentgen therapy were permanent; symptoms did not recur during the eighteen months subsequent to the treatment.

Spontaneous improvement being known to occur,[26] the results of roentgen therapy were tested by submitting the patients to the following experiment. The roentgen therapy equipment used included a water-cooling system with an electric pump making a loud humming sound. This pump could be operated independently, without generating roentgen rays. It was impossible for the patients to know whether they received radiation or not. Of the 8 persons tested in the experiment, one stated that he had "perhaps" felt some relief from pain after a series of pseudotreatments. The other 7 patients felt no improvement after pseudotherapy, but experienced complete relief from symptoms after real roentgen treatment. This would seem to indicate that the effect of radiation therapy in these cases is not psychologic, but caused by the roentgen rays.* Since, as mentioned above, no other mode of treatment was given during and after roentgen therapy, the results cannot be attributed to some concurrent therapeutic measures.

It is difficult to understand the mechanisms responsible for this therapeutic effect. In a large number of patients with rheumatoid arthritis of peripheral joints treated from 1927 to 1941 with roentgen rays of variable penetrations and doses, directed to the joints themselves, the vas-

* Two months after the present paper had been accepted for publication an article dealing with similar experiments by C. J. Smyth, R. H. Freyberg, and W. S. Peck, appeared in *J. Am. M. Ass.*, 1941, *116*, 1995–2001. With a slightly different experimental method, these authors found that mental factors do not play an important rôle in the treatment of Strümpell-Marie disease. They recorded excellent results of roentgen therapy with higher penetrations and larger doses than those which I used.

cular system of the extremities, or the vertebral segments which correspond to the nerves supplying the involved peripheral joints, no improvement of symptoms or lesions could be observed by the writer. One may therefore be inclined to ascribe the favorable influence of roentgen therapy upon arthritis of the apophyseal joints to the analgesic effect of roentgen irradiation. But a surprising change of the roentgenologic appearances was observed to occur in the apophyseal joints of 4 patients after treatment (Fig. 3 and 9). The joint spaces, clouded and apparently filled with bone before treatment, became radiolucent and clearly defined after treatment. Perhaps the radiation therapy caused a calcification or ossification of the capsule to disappear, in analogy to the effect upon calcifications in bursae and tendons. A spontaneous retrogression in untreated patients did not occur. No definite change in the roentgen findings took place after treatment in advanced cases. It seems that, in addition to its analgesic effect, roentgen therapy has a favorable action upon the articular lesion itself.

These observations, although necessarily small in number because incipient stages are so rarely observed, show that cure consisting of disappearance of symptoms as well as lesions can be achieved by means of roentgen therapy at early stages of Strümpell-Marie disease. At more advanced stages, relief from pain resulting in subjective improvement of mobility can be obtained, but the anatomical condition can no longer be improved. The lesion is reversible at early stages, but irreparable when the articular cartilage is severely damaged.[16] Hence the need for an early diagnosis.

The practical conclusion which can be drawn from this study may be worded as follows. When a patient suffers from pain in the back or neck and the mobility of the involved region is limited for more than a few weeks, a roentgen examination of the spine, including a study of the apophyseal joints with an adequate technique, should be made, even when the symptoms subside temporarily. A male between twenty and thirty years old should be examined with particular care in the presence of these symptoms; but both sexes and all age groups may be affected. If the roentgen findings suggest an incipient rheumatoid arthritis of one or a number of apophyseal joints, roentgen therapy with small doses and intermediate penetration should be instituted at once. To wait for ossification to appear in the vertebral ligaments or for the sacroiliac joints to become involved in order to confirm the diagnosis of Strümpell-Marie disease means depriving the patient of the one chance of cure he has at the present stage of our knowledge: once the lesion has advanced beyond the reversible stage, the gradual transformation of a healthy young adult into an invalid stricken with pain and immobility can rarely be halted.

XV. SUMMARY

1. Clinical and roentgenologic observations, verified by control series, showed that pain in the spine associated with limitation of vertebral movements is usually caused by lesions of the apophyseal joints.

2. Lesions of the apophyseal joints conform to the conception of arthritis both anatomically and on the basis of their clinical manifestations. Lesions of the vertebral symphyses—the joints formed by the intervertebral discs—have neither the anatomic nor the clinical characters of arthritis.

3. The lesion associated with the clinical syndrome of Strümpell-Marie disease consists in a rheumatoid arthritis of the apophyseal joints (atrophic spondylarthritis). Rarefaction of vertebral bodies and ossification of vertebral ligaments may become superadded, but do not always occur; when present, they are signs of an advanced stage of the disease.

4. Like atrophic arthritis of the peripheral joints, atrophic spondylarthritis, although it is a potentially ankylosing lesion, does not lead in every case to bony ankylosis between the facets. Like atrophic arthritis of peripheral joints, it may become quiescent or arrested before ankylosis takes

place, and features of hypertrophic arthritis may then become superimposed upon the original lesion.

5. Pain in the spine and limitation of vertebral movements occur at incipient as well as at advanced stages of atrophic spondylarthritis. They are caused by the lesion of the apophyseal joints and do not depend upon secondary changes such as ossification of ligaments or rarefaction of vertebral bodies.

6. At initial and early stages of atrophic spondylarthritis, complete cure, with disappearance of the lesions roentgenologically, can be achieved by roentgen therapy with small doses and intermediate penetration. At more advanced stages, the lesion itself is irreparable, but roentgen therapy is useful in controlling pain and in producing thereby a subjective improvement of vertebral mobility.

7. The need for an early diagnosis based on roentgen examination of the apophyseal joints is stressed in view of these limitations of therapy.

Acknowledgments. Mr. R. Lawford Knaggs, formerly Professor of Surgery in the University of Leeds, has taken great interest in this study and has encouraged the publication of the findings although they differ from those which he recorded in his own articles. The trend of the presentation was influenced by advice received from Dr. Stuart Carter Dodd, Professor of Sociology, and Dr. Edmund Mayer, Professor of Pathology, American University of Beirut. Dr. George W. Saleeby and Mr. Karnig M. Sarrafian, Department of Roentgenology, have cooperated in collecting and recording the data. The writer is sincerely indebted to them all.

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CHONDRODYSTROPHIA CALCIFICANS CONGENITA

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CONRADI,[2] in 1914, first described a condition of this type and stated that he could find no case of similar type in the literature. Although somewhat similar instances have since been reported under a varied nomenclature, which shows a tendency toward a classification under chondroplasia, the generic term chondrodystrophia appears to be more logical and we have only added the two descriptive adjectives to define this group of sporadically reported cases.

Ours is apparently the first example in which a familial and congenital characteristic is proved and in which opportunity has been afforded to investigate 4 cases over a period of time, together with postmortem examinations of the material in one instance.

In October, 1938, there were submitted to us roentgengograms of the chest and long bones in the case of a male child aged ten months (Case I) with a requisition which read under the caption "Clinical Remarks—the twin of this one died suddenly last night." In this case we reported a slight haziness in both lung fields due to an acute respiratory infection and then with reference to the long bones, flaring of the distal ends of the ulnae and tibiae, together with the mottled granular appearance in the ankles, wrists and other joints which in contour follows that of the bony structures in normal ossification, but presents angular densifications rather than rounded densities. This child also showed clinical manifestations of a pneumonia, together with numerous red cells in the urine, with practically no other abnormalities. The temperature rose to 103° F. on the second day, then subsided to normal on the fourth day. Blood count was 3,500,000 erythrocytes, 17,000 leukocytes, 60 per cent hemoglobin, normal differential. The blood count returned to normal in about one week, and the patient has been clinically normal ever since.

Permission was granted to exhume the deceased male twin (Case II) and films were made. These showed joint changes exactly similar to those of the living twin. All organs were examined grossly and microscopically and the cause of death from the history and microscopic sections was attributed to a pneumonia of the right lower lobe. From the history it would appear that this child had been ill for several days previously. On the basis of a possible metallic poisoning, the organs were subjected to chemical analysis and proved negative for the presence of bismuth, arsenic or lead.

The bones of the ankle were removed together with masses of cartilaginous material for histologic study. The microscopic report is as follows: "Sections show an increase of fibrous tissue of periosteal character. Directly under this periosteum a formation of cartilage is noted. The deeper cells are acquiring a cartilaginous character. The deepest layers of cells form osteoid tissue, which is partly calcified. There is no evidence of malignancy."

Several hours were spent in delving into a history of the entire family which included an older child aged two and a half (Case IV), father, mother and both grandmothers, with special reference to type of feeding. The mother was a nurse, who gave us intelligent information but no relevant points were obtained. About two weeks later she was delivered of another male child (Case III) which shows the same changes. A two and a half year old girl, also examined, shows normal bony structures, except for a few punctate densities in both wrists and ankles which suggest that she may previously have had the same changes. The parents show normal bony structures in these areas.

We have been able to follow these chil-

FIG. 1. Case 1. Male living twin at ten months, October, 1938, showing calcium deposits in hip joints and knees.

dren for almost four years. Apparently these abnormal calcifications are marked at birth and disappear by the age of about three years. All were subjected to calcium, phosphorus, cholesterol and phosphatase determinations, blood counts and serologic studies, and no unusual features were discovered. The roentgen studies of all other bony structures show no evidence of dwarfism or cretinism, and rickets and scurvy are ruled out by the dietary history, the chemical findings and the roentgen studies of other bony structures.

Conradi was able to observe his patient roentgenologically and clinically and also made histologic examinations. His patient was a child, female, three months old on admission, suffering from "haematoma of the scalp and head." The femurs showed thickened epiphyses with thin diaphyses. The right was shorter than the left. All four extremities were strikingly shorter and thicker than normal. Fingers and toes were thick and short. No chemical evidences of syphilis. Roentgen findings: The changes were most marked in the distal ends of the femurs and in the tarsal bones. The distal femoral epiphyses were stippled, likewise the tarsal bones, with peculiar shot-like shadows. The distal tibial and fibular epiphyses were affected also while the upper tibial and fibular epiphyses were only slightly involved.

Tisdall and Erb[11] in 1924, reported 2 cases, the first of which at five weeks presented roentgenographically "peculiar irregular calcareous deposits in the epiphyses at both ends of the humeri, the proximal ends of the radii, ulnae, tibiae, fibulae and distal ends of the femora. The patellae were practically outlined by these deposits. Unfortunately, no films were made of other areas and there were no deposits in the skin or muscles." Films of the elbows and knees are shown which in many respects resemble

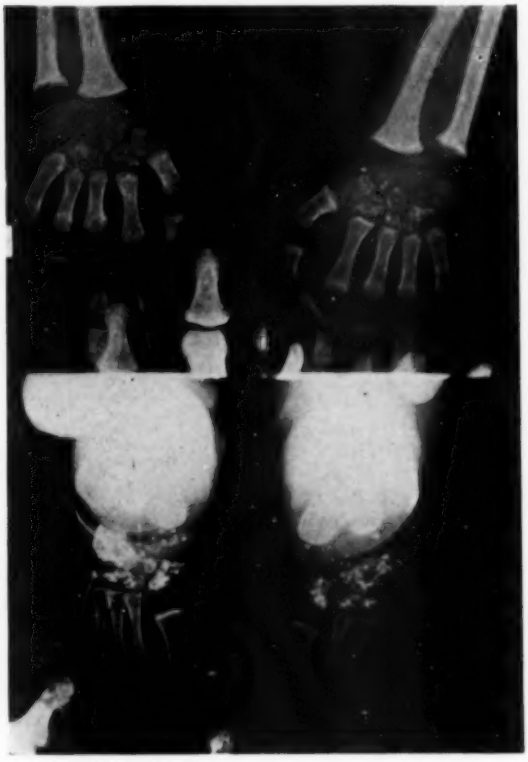

FIG. 2. Case 1. Living twin at ten months. Note calcific deposits in wrists and ankles.

the present cases. Microscopic sections of the patella show a vacuolated appearance in which nuclei have disappeared. There are calcareous deposits in areas of degenerated connective tissue. Here, however, we are dealing also with a syphilitic infection which may account for this degeneration. Blood calcium was 9.3 and 9.7 mg. per 100 cc. and phosphorus 4.5 and 4.4 mg. per 100 cc.

Fig. 3. Case II. Male deceased twin at ten months. October, 1938.

Geyman[4] differentiates the appearance of luetic lesions of the congenital type and calls attention to Kaufmann's description of three forms of chondrodystrophy, hypoplastic, malacic and hyperplastic, and also remarks that chondrodystrophy is frequently confused with cretinism, although occasional cases of unilateral chondrodystrophia are seen.

Hünermann[5] in 1931 reported a case of a female child, aged three weeks, whom he had the opportunity of observing for almost two years. The roentgen findings were innumerable dense, small, stippled shad-

Fig. 4. Microscopic section from ankle of Case II.

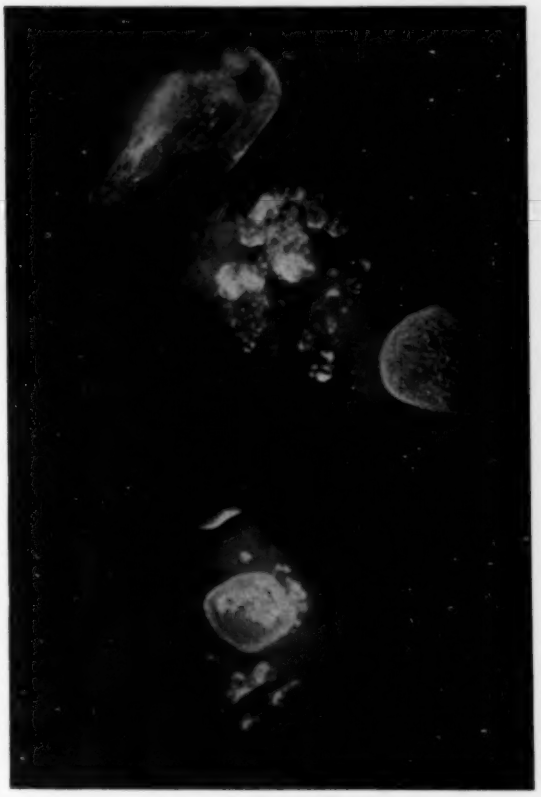

Fig. 5. Roentgenograms of removed sections from ankles and wrists in Case II.

FIG. 6. Case 1 at twenty months. Note gradual disappearance of these deposits.

ows, of varied shapes, in the epiphyses of the extremities as well as along the spinal column and in the pelvis. The skull and facial bones were not affected. These stippled shadows were found in the proximal epiphyses of the humeri, the proximal epiphyses of each radius, the distal end of the left humerus and the proximal end of the right ulna. The right femur was shorter than the left, the heads and neck of each femur were affected, the distal epiphyses of the femurs, the upper epiphyses of the tibias, distal epiphyses of the tibias and the bones of each ankle joint. The carpal bones showed a few stippled shadows. The bony structure of the shafts throughout was normal. Hünermann quotes Conradi, Dietrich and Wiskott, all of whom published similar cases. The roentgen findings are not those of typical chondrodystrophia fetalis or achondroplasia in that the thickened shafts of the long bones due to endosteal and periosteal change are not present. There is also no shortening of all long bones of the extremities. There is also no broadening of the diaphyseal ends.

Hünermann's case was identical clinically and roentgenologically with those of Conradi and Dietrich. He described Conradi's histological findings. Based on these histological findings, Conradi decided the disease process was an abortive form of chondrodystrophy or achondroplasia.

In 1938, Reilly and Smyth[7] described the stippled epiphyses of congenital hypothyroidism. Although the most typical cases described showed hypothyroidism as a most evident factor, it is stated that it may also occur without hypothyroidism. Their article also emphasizes the similarity to Legg-Calvé-Perthes' disease. Such a similarity is not suggested in our cases, and the

FIG. 7. Case III. Male, aged ten days. December, 1938. Appearance of ankles and wrists proves that these changes are present at birth.

evidence of hypothyroidism is entirely absent. The stippling is confined to the epiphyseal centers alone and is not present in the cartilage.

Maitland[6] reports the case of a female child, three days old, weighing 7 pounds, with enlarged knee and elbow joints, somewhat spastic, showing marked developmental changes in the cervical and dorsal vertebrae together with shortening of the extremities and punctate calcifications in the knees and elbows but with very little in the wrists and ankles. A previous child born in 1935, in the same family, had similar changes and lived only nine months. In these cases there is a marked element of developmental anomaly, since the father also shows absence of certain phalanges in the hands. This is apparently a story of transmitted notochordal anomalies.

Attention is directed to the fact that in all previous reports of a disturbance of this nature, there were evident extenuating factors such as developmental variants, syphilis, cretinism, hypothyroidism. In our cases the children are apparently normal in every other respect living under ordinary conditions of life. We have been able to observe these changes without medication or attempt to vary this abnormal condition.

Fig. 8. Case iv. Female, aged two and one-half years. Shows persistence of calcific deposits.

Fig. 9. Case iv, aged four years. Deposits have practically disappeared.

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Vol. 49, No. 1

THE PREVENTION OF IRRADIATION SICKNESS

USE OF VITAMIN B_1 IN ROENTGEN THERAPY

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THE symptoms of malaise, anorexia, nausea, and vomiting, associated with or following irradiation with roentgen rays or the gamma rays of radium have been called roentgen or radium sickness. This illness has been a disturbing complication since the beginning of the massive dose or intensive type of roentgen and radium therapy. Many theories have been advanced as to the cause of this sickness, and considerable research work has been done, but as yet, the exact nature of the changes producing the constitutional symptoms have not been determined.

The symptoms of irradiation sickness may start shortly after or some hours after a single moderate or large dose of radiation, or in some cases the day following the treatment; when the fractional method of giving radiation daily in small or moderate sized doses is used, the sickness may not develop until the second week or later. There is marked variation in the susceptibility of individuals, and in the severity of symptoms. In mild cases there is general languor and malaise, with anorexia and slight nausea; in moderately severe cases there is more nausea with occasional vomiting; in the more severe cases there is marked nausea with frequent vomiting, weakness and prostration. Usually there is constipation, probably due to the low food intake, but in a few cases diarrhea is present, which may be a part of the irradiation sickness but more frequently is due to the direct effect of the irradiation on the intestinal tract, in abdominal and pelvic cases. Irradiation of the abdomen, pelvis, breast and lower thorax are more likely to cause irradiation sickness than treatment of other parts of the body.

Some of the theoretical causes of roentgen sickness that have been suggested are:

(*a*) gases produced by the corona and high tension electric field;
(*b*) an electric field surrounding the body of the patient;
(*c*) chemical changes produced in the body by irradiation;
(*d*) general influence of irradiation on the body and absorption of the products of cell destruction;
(*e*) irradiation effects on certain organs of internal secretion;
(*f*) nervous strain and psychic influences;
(*g*) destruction of intestinal mucosa.

Pfahler[12,13] in 1916 and 1918 reported his observations and experiments relating to the cause and prevention of roentgen sickness. His experiments with guinea pigs indicated some toxic element in the air from around the tube. By protecting his patients from the contaminated air and providing fresh air with oxygen inhalations during treatments, he was able to reduce the incidence of roentgen sickness to about one-third of the previous frequency.

It seems very probable that there was a psychic factor in some of the cases of roentgen sickness; unpleasant odors may increase nausea, regardless of the primary cause; in the past, patients often complained of the odor in the treatment room, and some of them became nauseated as soon as they entered the room. It is probable that the incidence of true roentgen sickness is the same with modern equipment as it was with the old type, and that the apparent reduction of incidence with modern equipment is due to the elimination of the false roentgen sickness cases which were due to psychic influences and the toxic effects of the gases generated around the high tension leads and the roentgen tube. Certainly such gases are not a factor in true irradiation sickness, as this frequently develops during radium therapy or during treatments with modern coronaless equipment.

Jones and Roth[9] found the effect of im-

proved ventilation only temporary and apparently more psychic then real; they did not find that acidosis was a factor in these cases; they noted that the region of the body treated was an important factor, and that irradiations of the abdomen, breast and lower thoracic areas were most likely to cause symptoms; they concluded that irritation of the vagus nerve was a cause of constitutional symptoms.

Béclère[2] considered, from a physiological standpoint, that the effects of irradiation on the nerves were the underlying cause of the symptoms; that the symptoms may be due to the effect of the rays on nerve endings or sympathetic ganglia, or that the ray caused the passage into the blood of some substance that has emetic properties. Béclère noted that the constitutional symptoms frequently followed irradiation of tumor masses which resolved rapidly, and stated that "from clinical data it would appear that the chief cause of the disturbance . . . is the passage into the blood stream of certain soluble substances, more or less toxic, resulting from the disintegration of normal and pathological cellular elements. To this must be added, . . . the direct effects of the penetrating rays upon the ganglionic nervous system of the viscera."

Doub, Bolliger and Hartman[3,4] studied the metabolic changes following roentgen therapy. Their equipment was arranged to avoid any effect from the gases or the high tension electric field, with no part of the high tension apparatus or roentgen tube in the room with the patient or experimental animal, and with a grounded metal shield between the subject and the high tension parts. From their observations on 23 patients and experiments on dogs, they reported:

(*a*) that there was an increase in the acid soluble phosphorus coincident with nausea, vomiting and alkalosis;
(*b*) no distinct change in the CO_2 combining power of the blood; they found alkalosis with initial depression of the hydrogen ion concentration;
(*c*) sugar content of the blood increased after irradiation, in dogs an immediate rise;
(*d*) marked decreases in amino acids of the blood, suggesting that the protoplasm of the irradiated cells remains intact during the early stages, and that there is increased enzymic activity producing deamidation with resultant increase in the blood sugar;
(*e*) marked decrease in non-protein nitrogen during the first hours with later increases of 75 to 100 mg. per 100 cc. of blood in dogs receiving a lethal or near lethal dose of roentgen rays;
(*f*) slight decrease in blood calcium, considered as probably secondary to the increased phosphorus;
(*g*) an immediate large increase in the phosphorus content of the blood, interpreted as an index of acute nuclear destruction.

From their findings they suggest that irradiation sickness is due to the immediate products of nuclear destruction.

Arons and Sokoloff[1] considered that the effect of irradiation on the reticulo-endothelial system was a factor in roentgen sickness; that a small dose of the rays stimulates the reticulo-endothelial cells, and that a larger dose inhibits or destroys the defense mechanism of this system.

Morgan[11] was of the opinion that roentgen sickness was due to too rapid administration of the rays in the massive dose technique, and advocated fractional doses, giving the required dosage in ten days to two weeks; in some cases he divided the daily dose, giving a fraction of the dose each hour from 9 A.M. to 6 P.M. He reported that roentgen sickness was generally not produced by such fractional dosage. Extreme fractionating of doses is not a practical method of therapy when many patients are to be treated and the total dose for each patient relatively large.

Various treatments for irradiation sickness have been proposed and tried. Some have been of value in improving the psychic and bodily comfort of the patient, such as the elimination of noxious gases and providing fresh air in treatment rooms;[13] the sedatives frequently employed have reduced the severity of the symptoms, but have increased the anorexia.

TABLE I

BRIEF REPORT OF EACH OF 122 CASES

Case No. and Patient	Age	Diagnosis	Duration of Treatment	No. of Portals; Size in cm.*	Total Dosage in Roentgens†	Medication; Comments‡
1. Mrs. N.B.	43	Menorrhagia	9-18-38 to 10- 8-38	2-15×15 (c)	1,600	Thiamin 6 mg.; nausea o; appetite good
2. Mrs. E.F.	50	Cancer uterine stump	10-25-38 to 11-29-38	6-10×15 (b)	10,200	Thiamin 6 mg.; liver; calc.; nausea o; appetite fair
Rules						
3. Miss L.B.	54	Cancer right breast, and skin metastases	10-27-38 to 11-30-38	3-10×15 1-10×10 (a)	8,000	Thiamin 6 mg.; liver; calc.; nausea o; appetite fair
			3- 9-39 to 4- 8-39	2-10×15 (a)	4,000	
			6- 7-39 to 6-27-39	3-10×15 (d)	6,210	
4. Mrs. L.E.R.	54	Cancer fundus uteri	10-27-38 to 11-23-38	6-10×15 (b)	10,200	Thiamin 6 mg.; liver; calc.; nausea slight; appetite fair
5. Mrs. G.H.	25	Cancer cervix uteri	10-28-38 to 11-15-38	4-10×15 (b)	6,100	Thiamin 6 mg.; liver; calc.; nausea o; appetite improved
6. Mrs. J.O.C.	60	Cancer cervix uteri	11-21-38 to 12-21-38	6-10×15 (b)	10,200	Thiamin 6 mg.; liver; nausea o; appetite poor
7. Mrs. C.H.D.	49	Cancer cervix uteri	11-21-38 to 12-20-38	6-10×15 (b)	10,200	Thiamin 6 mg.; liver; calc.; nausea o; appetite improved
8. Mrs. W.L.H.	71	Cancer right breast	11-22-38 to 12-29-38	3-10×15 2- 8×10 (a)	9,000	Thiamin 6 mg.; liver; calc.; nausea o; appetite fair
9. Mr. D.T.R.	53	Cancer lung	11-21-38 to 12-21-38	5-10×15 (c)	12,250	Thiamin 6 mg.; liver; codeine (for pain); nausea o; appetite poor
10. Mrs. A.K.R.	65	Cancer bladder	11-29-38 to 12-27-38	2-10×15 1-10×10 1- 8×10 (f)	9,400	Thiamin 0.6 mg. (error); liver; calc.; nausea severe; thiamin 9 mg.; nausea o after 2 days; appetite fair
11. F.M. (F)	51	Cancer left breast	12- 2-38 to 1- 7-39	4-10×15 1- 8×10 (a)	9,900	Thiamin 6 mg.; calc.; nausea o; appetite good

* Voltage, filtration and focal skin distance indicated as:

(a) 200 kv., 0.5 mm. Cu, 1.0 mm. Al; 50 cm. focal skin distance;
(b) 200 kv., 0.5 mm. Cu, 1.0 mm. Al; 70 cm. focal skin distance;
(c) 200 kv., 1.0 mm. Cu, 1.0 mm. Al; 50 cm. focal skin distance;
(d) 140 kv., 0.25 mm. Cu, 1.0 mm. Al; 50 cm. focal skin distance;
(e) one portal, 15×15 cm., (d); other portals (a);
(f) 200 kv., 0.42 mm. Sn, 0.25 mm. Cu, 1.0 mm. Al; 50 cm. focal skin distance;
(g) 220 kv., 1.05 mm. Sn, 0.25 mm. Cu, 1.0 mm. Al; 50 cm. focal skin distance.

† Measured in air, without backscatter.

‡ Amount of thiamin listed is the daily dosage of thiamin chloride. "Liver" indicates concentrated liver extract (usually reticulogen), containing thiamin chloride, 0.5 cc. intramuscularly, three times weekly. "Calc. indicates calcium salts, usually compound gluconate and dicalcium phosphate, 1 gram, three times daily.

TABLE I—*Continued*

Case No. and Patient	Age	Diagnosis	Duration of Treatment	No. of Portals; Size in cm *	Total Dosage in Roentgens†	Medication; Comments‡
12. Mr. E.D.B.	46	Sarcoma thyroid	12-21-38 to 12-31-38	2- 9×12 (f)	6,000	Thiamin 0; nausea moderate; thiamin 6 mg.; calc.; nausea 0 after 2 days
			4-13-39 to 5-20-39	1- 8×10	2,450	
13. Mrs. E.K.	55	Cancer corpus uteri	12-20-38 to 1-19-39	6-10×15 (b)	11,400	Thiamin 6 mg.; liver; nausea 0; appetite fair
14. Mr. J.V.R.	54	Cancer floor of mouth, and glands of neck	12-27-38 to 1-27-39	2- 6× 8 1-6 cm. (f)	13,000	Thiamin 6 mg.; liver; nausea slight; appetite poor (dysphagia)
			5- 5-39 to 5-24-39	2-10×10 (f)	4,400	
15. Mrs. V.S.	60	Cancer left breast, preoperative; postoperative	12-19-38 to 12-30-38	3-10×15 1- 8×10 (a)	3,600	Thiamin 6 mg.; liver; calc.; nausea 0; appetite fair
			2-22-39 to 3-12-39	3-10×15 1- 8×10 (a)(d)	6,000	
16. Mr. J.T.W.	67	Cancer glands right neck	1- 6-39 to 2- 6-39	1-10×10	5,000	Thiamin 6 mg.; liver; nausea 0; appetite good
			9-30-39 to 10-25-39	1- 8×10 2- 6 cm. (f)	2,700 6,000	
17. Mr. J.E.E.	50	Lymphoblastoma of stomach	1- 5-39 to 1-30-39	2-15×15 (g)	8,200	Thiamin 6 mg.; liver; calc.; nausea slight
18. Mrs. R.W.J.	46	Cancer cervix uteri	2- 8-39 to 3- 4-39	6-10×15 (b)	10,200	Thiamin 6 mg.; liver; calc.; nausea slight, occasionally; appetite fair
19. Mrs. B.H.	48	Cancer corpus uteri	2- 9-39 to 3- 4-39	6-10×15 (b)	10,200	Thiamin 6 mg.; liver; calc.; nausea 0; appetite fair
20. Mrs. W.A.G.	56	Cancer cervix and corpus uteri	3- 6-39 to 3-28-39	6-10×15 (b)	10,200	Thiamin 6 mg.; liver; calc.; nausea 0; appetite fair
21. H.B. (F)	30	Cancer cervix uteri	3- 7-39 to 4- 3-39	6-10×15 (b)	10,200	Thiamin 6 mg.; liver; nausea 0; appetite good
22. Mrs. J.P.C.	56	Cancer right breast postoperative	3-14-39 to 4-10-39	3-10×15 1- 8×10 (a)	7,200	Thiamin 0, 2 weeks; nausea, moderate; thiamin 6 mg.; nausea 0; appetite improved
23. Mrs. B.P.	57	Cancer vulva and inguinal metastases	3-14-39 to 3-30-39	1-15×15 1- 8×10 1- 5 cm.	4,000 6,000	Thiamin 6 mg.; liver; calc.; nausea 0; appetite good
			4-25-39 to 5-22-39	1-10×10 (f)		
24. Mrs. J.A.G.	45	Cancer right breast; sterilization	3-20-39 to 5- 4-39	3-10×15 1- 8×10 4-10×15 (a)(c)	6,600 3,200	Thiamin 6 mg.; liver; nausea 0; appetite fair

TABLE I—*Continued*

Case No. and Patient	Age	Diagnosis	Duration of Treatment	No. of Portals; Size in cm.*	Total Dosage in Roentgens†	Medication; Comments‡
25. Mr. H.L.H.	65	Cancer in colostomy, from cancer of colon	3-27-39 to 4-19-39	1-10×15 (a) 2- 6× 3 (100 Kv–2. Al)	2,500 4,000	Thiamin 6 mg.; liver; nausea o; appetite good
26. Mrs. A.P.	51	Cancer cervix uteri	3-29-39 to 4-25-39	6-10×15 (b)	10,200	Thiamin 6 mg.; liver; nausea slight; appetite good
27. Mrs. L.B.	79	Cancer left breast	3-27-39 to 4-20-39	3-10×15 1- 8×10 (a)	6,450	Thiamin 6 mg.; liver; calc.; nausea o; appetite fair
28. Mrs. L.B.	65	Cancer left breast	4- 3-39 to 5- 6-39	3-10×15 1- 8×10 (a)	8,200	Thiamin 6 mg.; liver; nausea o; appetite very good
29. Mr. J.L.C.	65	Cancer prostate	4-17-39 to 5-13-39	3-10×10 1- 8×10 (f)	10,000	Thiamin 6 mg.; liver; nausea o; appetite fair
30. Mrs. W.W.U.	41	Cancer cervix uteri	5- 1-39 to 5-27-39	6-10×15 (b)	9,600	Thiamin 6 mg.; liver; nausea moderate (colitis prior to roentgen therapy)
31. Mrs. H.L.S.	77	Cancer left breast	5-12-39 to 6-20-39	3-10×15 1- 8×10 (a)	9,000	Thiamin 9 mg.; liver; calc.; nausea o; appetite good
32. Mrs. M.G.W.	47	Cancer left breast; sterilization	5-22-39 to 6-22-39	3-10×15 1- 8×10 4-10×15 (a)(c)	7,800 3,200	Thiamin 6 mg.; liver; calc.; nausea o; appetite very good
33. Mrs. E.H.M.	43	Cancer cervix uteri	6- 3-39 to 6-30-39	6-10×15 (b)	10,200	Thiamin 6 mg.; liver; nausea o; appetite poor (morphine addict)
34. Mr. E.R.S.	49	Cancer pelvis, metastatic	6-12-39 to 7-14-39	6-10×15 (b)	11,700	Thiamin 6 mg.; liver; nausea slight; appetite fair
35. Mrs. E.H.H.	62	Cancer cervix uteri	6-12-39 to 7-10-39	6-10×15 (b)	10,200	Thiamin 6 mg.; liver; nausea o; appetite good
36. V.W. (F)	40	Cancer right breast	6-13-39 to 7-24-39	4-10×15 1- 8×10 (a)	10,350	Thiamin 6 mg.; calc.; nausea slight; appetite fair
37. Mr. J.A.W.	64	Cancer right buccal mucosa	6-27-39 to 7-28-39	2- 6× 8 1- 6 cm. (f)	11,150	Thiamin 9 mg.; nausea o; appetite very good
38. Mrs. J.B.	50	Cancer left breast, postoperative, recurrent	7- 5-39 to 7-27-39	1-10×13 (d)	2,500	Thiamin 6 mg.; nausea o; appetite fair
39. Mrs. L.D.T.	65	Cancer cervix uteri	7-11-39 to 8- 9-39	6-10×15 (b)	10,200	Thiamin 6 mg.; liver; calc.; nausea o; appetite good
40. Miss H.L.W.	50	Bilateral cancer of breast, preoperative, postoperative	7-17-39 to 7-29-39 8-28-39 to 10- 4-39	4-10×15 2-15×15 2- 8×10 2-10×15 2-15×15 2- 8×10 (a)(e)	7,200 9,600	Thiamin 9 mg.; liver; calc.; nausea o; appetite good

TABLE I—*Continued*

Case No. and Patient	Age	Diagnosis	Duration of Treatment	No. of Portals; Size in cm.*	Total Dosage in Roentgens†	Medication; Comments‡
41. Mrs. G.C.B.	47	Cancer cervix uteri	7-17-39 to 8-14-39	6-10×15 (b)	10,200	Thiamin 6 mg.; liver; calc.; nausea o; appetite good
42. Mr. G.B.T.	71	Cancer bladder	7-17-39 to 8-16-39	3-10×10 1- 8×10 (f)	10,000	Thiamin 6 mg.; liver; calc.; nausea o; appetite good
43. Mrs. S.W.Z.	49	Cancer left breast	8-15-39 to 9-12-39	3-10×15 1- 8×10 (a)	7,800	Thiamin 6 mg.; liver; nausea o; appetite very good
44. Mrs. F.B.P.	71	Cancer left breast	7-25-39 to 8-12-39	1-10×15 2- 8×10 1- 6× 8 (a)	4,800	Thiamin 6 mg.; liver; nausea o; appetite poor
45. Mrs. F.W.H.	79	Cancer right breast	8-21-39 to 9-18-39	2-10×15 1- 8×10 (a)	6,450	Thiamin 9 mg.; liver; nausea o; appetite good
46. Mr. J.S.	61	Cancer metastatic neck	8-25-39 to 9-22-39	2- 8×10 (f)	6,000	Thiamin 6 mg.; codeine (for pain); nausea o; appetite poor
47. Mrs. W.P.C.	57	Cancer lower lip; metastases in neck	9- 5-39 to 10- 7-39	2- 6× 8 2- 6 cm. (f)	11,200	Thiamin 6 mg.; liver; nausea o; appetite poor
48. Mr. C.B.	73	Cancer larynx	9-11-39 to 10-2-39	2- 8×10 (f)	7,000	Thiamin 6 mg. increased to 9 mg.; nausea o; appetite improved
49. Mrs. M.T.	48	Cancer cervix; recurrent	9-14-39 to 10-18-39	6-10×15 (b)	10,200	Thiamin 6 mg.; liver; nausea o; appetite very good
50. Mrs. E.B.S.	83	Cancer right breast	9-15-39 to 10-16-39	2-10×15 2-10×10 1- 8×10 (a)	9,000	Thiamin 6 mg.; liver; calc.; nausea o; appetite good
51. V.B. (F)	48	Cancer cervix uteri	9-18-39 to 10-18-39	6-10×16 (b)	10,200	Thiamin 6 mg.; liver; calc.; nausea o; appetite improved
52. Mr. J.B.	28	Cancer metastases in neck	9-25-39 to 11- 1-39	4- 8×10 (a)	12,000	Thiamin 6 mg.; liver; nausea o; appetite good
53. Mrs. J.F.	36	Cancer left buccal mucosa	9-28-39 to 10-30-39 11- 7-39 to 11-28-39	1- 8×10 2- 6× 8 (f) 1- 3 cm. (a)	9,000 3,500	Thiamin 6 mg.; liver; nausea o; appetite poor
54. Mr. H.A.C.	53	Cancer right forearm, with epitrochlear and axillary metastases	10-16-39 to 12-14-39	3-10×15 3-10×10 1- 8×10 (a)(f)	16,000	Thiamin 6 mg.; nausea o; appetite good
55. Mrs. J.S.	66	Cancer right breast	10-16-39 to 11-11-39	3-10×15 1- 8×10 (a)	9,000	Thiamin 9 mg.; liver; calc.; nausea o; appetite improved

TABLE I—*Continued*

Case No. and Patient	Age	Diagnosis	Duration of Treatment	No. of Portals; Size in cm.*	Total Dosage in Roentgens†	Medication; Comments‡
56. A.H. (F)	65	Cancer cervix uteri	10-16-39 to 11-15-39	4-10×15 (c)	7,800	Thiamin 6 mg.; liver; nausea o; appetite fair
57. Mrs. K.B.M.	33	Cancer cervix uteri	10-19-39 to 11-15-39	6-10×15 (b)	10,200	Thiamin 6 mg.; liver; calc.; nausea moderate; thiamin increased to 9 mg.; nausea relieved; appetite improved
58. Mrs. I.B.	49	Cancer left femur metastatic from breast	10-24-39 to 11-29-39	3-15×20 (f)	7,200	Thiamin 6 mg.; liver; calc.; nausea o; appetite fair
59. L.W. (F)	58	Cancer left breast	10-31-39 to 11-29-39	3-10×15 1- 8×10 (a)	7,200	Thiamin 6 mg.; nausea o; appetite good
60. Mrs. M.J.B.	54	Cancer cervix uteri	11- 7-39 to 12-30-39	6-10×15 (b) 1- 3 cm. (a)	9,900 5,820	Thiamin 6 mg.; liver; calc.; nausea slight; thiamin increased to 9 mg.; nausea o; appetite improved
61. Mrs. A.O.S.	56	Cancer cervix uteri	11- 8-39 to 12-11-39	6-10×15 (b)	10,200	Thiamin 6 mg.; liver; calc.; nausea o; appetite fair
62. Mr. A.V.P.	60	Cancer bladder	11- 9-39 to 12-11-39	3-10×10 1- 8×10 (f)	10,000	Thiamin 6 mg.; liver; nausea o; appetite good
63. Mrs. F.H.S.	45	Cancer corpus uteri	11-13-39 to 12- 9-39	6-10×15 (b)	10,200	Thiamin 6 mg.; liver; calc.; nausea o; appetite very good
64. Mrs. J.E.E.	36	Cancer cervix uteri	11-27-39 to 12-23-39	6-10×15 (b)	10,200	Thiamin 6 mg.; liver; nausea o; appetite improved
65. Mr. J.S.E.	66	Sarcoma testis, with inguinal and pulmonary metastases	12-13-39 to 1-15-40	4-15×15 1-15×20 (c)	4,500	Thiamin 6 mg.; liver; nausea o; appetite poor
66. Mrs. F.H.	60	Cancer left breast, preoperative and postoperative	12-13-39 to 12-27-39 1-22-40 to 2-12-40	3-10×15 1- 8×10 (a) 1-15×15 1- 8×10 (e)	3,600 3,000	Thiamin 6 mg.; nausea o; appetite good
67. Mrs. H.H.A.	40	Cancer right breast, postoperative; sterilization	12-18-39 to 1-12-40 1-15-40 to 2-22-40	1-10×15 1-15×15 1- 8×10 (e) 2-15×15 (c)	5,400 2,200	Thiamin 6 mg.; liver; nausea moderate after pelvic treatments; appetite fair
68. Mrs. J.C.D.	59	Cancer left breast, preoperative and postoperative	1-15-40 to 1-27-40 3- 4-40 to 3-20-40	3-10×15 1- 8×10 (a) 1-10×15 1-15×15 1- 8×10 (e)	3,600 4,500	Thiamin 6 mg.; liver; nausea o; appetite good

TABLE I—*Continued*

Case No. and Patient	Age	Diagnosis	Duration of Treatment	No. of Portals; Size in cm.*	Total Dosage in Roentgens†	Medication; Comments‡
69. Mrs. C.C.F.	66	Cancer larynx	2- 5-40 to 3- 2-40	2- 6× 8 (f)	7,000	Thiamin 6 mg.; nausea slight; appetite poor
70. Mrs. M.D.P.	60	Cancer cervix uteri	2- 5-40 to 3- 2-40	6-10×15 (b)	10,200	Thiamin 6 mg.; liver; calc.; nausea o; appetite fair
71. Mrs. T.M.	50	Cancer left breast, post-operative; sterilization	2-26-40 to 3-22-40	2-10×15 1-15×15 1- 8×10	6,600	Thiamin 6 mg.; liver; nausea o; appetite improved
				2-15×15 (e)(c)	1,800	
72. Mr. O.H.C.	50	Cancer nose, face, left ear, and metastases in neck	2-12-40 to 3- 2-40	1- 6× 8 1- 7× 8 (f)	6,600	Thiamin 6 mg.; nausea o; appetite improved
			3-19-40 to 4- 5-40	1- 8×10 (a)	2,500	
73. Mrs. J.B.A.	57	Cancer cervix uteri	2-19-40 to 3-16-40	6-10×15 (b)	10,200	Thiamin 6 mg.; liver; calc.; nausea slight; appetite fair
74. Mrs. M.F.	58	Cancer corpus uteri	2-27-40 to 3-29-40	6-10×15 (b)	10,200	Thiamin 6 mg.; liver; nausea o; appetite good
75. Mrs. P.A.	64	Cancer of bladder	3- 4-40 to 4-11-40	3-10×10 (f)	7,500	Thiamin 9 mg.; liver; nausea o; appetite good
76. Mrs. M.E.D.	77	Cancer of tongue and floor of mouth	3-13-40 to 4-11-40	2- 6× 8 (f)	6,000	Thiamin 9 mg.; liver; nausea o; appetite fair
77. Mr. L.H.S.	44	Cancer of lung and mediastinum	3-18-40 to 4-29-40	2-10×20 3-10×15 2- 8×10 (c)	15,450	Thiamin 9 mg.; liver; nausea o; appetite improved
78. Mr. S.H.D.	65	Cancer of neck, secondary to lupus	3-18-40 to 4- 8-40	1-10×12 (f)	3,000	Thiamin 6 mg.; nausea o; appetite fair
79. Mrs. J.G.T.	60	Cancer of bladder	3-27-40 to 4-26-40	3-10×10 (f)	7,200	Thiamin 9 mg.; liver; nausea slight; appetite fair
80. Mrs. T.B.S.	50	Cancer right breast; sterilization	4- 2-40 to 5-17-40	3-10×15 1- 8×10 (a)	7,800	Thiamin none at start; nausea moderate; thiamin 9 mg.; nausea o; appetite improved
				2-15×15 (c)	1,800	
81. Dr. C.W.D.	63	Prostatic hypertrophy	4- 5-40 to 5- 3-40	2-10×15 (b) 1-12×12 1- 8×10 (f)	8,200	Thiamin 9 mg.; liver; did not take full amount, developed nausea; resumed full dosage, nausea o; appetite improved
82. Mrs. I.B.	69	Cancer cervix uteri	4- 6-40 to 5- 3-40	6-10×15 (b)	10,200	Thiamin 9 mg.; liver; calc.; nausea o; appetite improved

TABLE I—*Continued*

Case No. and Patient	Age	Diagnosis	Duration of Treatment	No. of Portals; Size in cm.*	Total Dosage in Roentgens†	Medication; Comments‡
83. Mrs. C.R.F.	48	Uterine fibroids	4- 8-40 to 5- 1-40	2-15×15 (c)	2,500	Thiamin 6 mg.; liver; nausea moderate 1 week; thiamin 9 mg.; nausea 0; appetite good
84. Mr. F.B.H.	45	Cancer of bladder (case not completed) (transferred)	4- 8-40 to 5- 1-40	2-10×15 1-12×12 (f)	4,800	Thiamin 6 mg.; liver; nausea slight; thiamin 9 mg.; nausea 0; appetite improved
85. Dr. J.W.M.	71	Cancer of bladder	4- 9-40 to 5- 8-40	2-10×15 1-12×12 1- 8×10 (f)	9,800	Thiamin 9 mg.; liver; nausea 0; appetite good
86. Mrs. W.N.H.	54	Cancer corpus and cervix uteri	4- 9-40 to 5- 6-40	6-10×15 (b)	10,200	Thiamin 9 mg.; liver; nausea moderate in 2nd week; relieved by thiamin 6 mg., hypo. q. 2 days; appetite improved
87. Mr. W.R.B.	56	Cancer of bladder	4-11-40 to 5-11-40	2-10×10 1-10×12 1- 8×10 (f)	9,600	Thiamin 9 mg.; liver; nausea 0; appetite good
88. Mrs. G.L.C.	72	Cancer left breast	4-29-40 to 5-28-40	3-10×15 1- 8×10 (a)	8,700	Thiamin 6 mg.; liver; nausea 0; appetite fair
89. Mrs. M.M.	39	Menorrhagia	5-13-40 to 5-31-40	2-15×15 (c)	1,800	Thiamin 6 mg.; nausea slight; appetite fair
90. Mrs. J.B.E.	63	Cancer right breast	5-24-40 to 6-21-40	3-10×15 1- 8×10 (a)	7,950	Thiamin 6 mg.; liver; nausea 0; appetite good
91. Mrs. A.W.R.	54	Cancer cervix uteri	6- 1-40 to 6-28-40	6-10×15 (b)	10,200	Thiamin 6 mg.; liver; nausea 0; appetite very good
92. Mr. W.P.F.	43	Cancer of lung	6-14-40 to 7-20-40	2-14×18 1-10×15 (c)	7,500	Thiamin 9 mg.; liver; nausea 0; appetite good
93. Mrs. I.M.S.	54	Cancer right breast, recurrent	6-17-40 to 7-15-40	3-10×15 1- 8×10 1- 6× 8 (a)	7,800	Thiamin 6 mg.; nausea 0; appetite good
94. Mrs. J.L.W.	58	Cancer right breast post-operative	6-17-40 to 7-12-40	1-10×15 1-15×15 1- 8×10 (e)	5,400	Thiamin 6 mg.; liver; nausea 0; appetite very good
95. Mr H.A.	58	Cancer esophagus	6-24-40 to 8-14-40	4-18×15 (f)	10,000	Thiamin 9 mg.; liver; nausea 0; appetite poor (dysphagia)
96. Mrs. J.H.D.	55	Cancer corpus uteri	6-25-40 to 7-20-40	4-10×15 (b)	7,400	Thiamin 9 mg.; liver; nausea moderate on 4th day; thiamin increased to 15 mg.; nausea relieved; appetite improved

TABLE I—*Continued*

Case No. and Patient	Age	Diagnosis	Duration of Treatment	No. of Portals; Size in cm.*	Total Dosage in Roentgens†	Medication; Comments‡
97. Mrs. H.H.H.	46	Cancer pelvis, metastatic from breast	7- 2-40 to 8- 8-40	6-10×18 (f)	10,800	Thiamin 9 mg.; liver; nausea 0; appetite good
98. Mr. C.W.M.	47	Mediastinal neoplasm	7- 6-40 to 8-28-40	2-12×18 (c)	4,800	Thiamin 9 mg.; liver; nausea 0; appetite good
99. Mrs. W.B.H.	59	Cancer cervix uteri	7- 8-40 to 8- 3-40	6-10×15 (b)	10,200	Thiamin 9 mg.; liver; nausea 0; appetite improved
100. Mrs. G.H.	63	Cancer cervix uteri	7-10-40 to 8- 7-40	4-10×15 (b)	8,400	Thiamin 9 mg.; liver; nausea 0; appetite good
101. Mr. E.H.	36	Seminoma, abdominal metastasis	7-22-40 to 8-29-40	4-15×20 (f)	6,000	Thiamin 9 mg.; liver; nausea 0 up to 8-20-40; 8-21-40 severe nausea with vomiting; 8-22-40 thiamin chloride 60 mg. by hypo.; 8-23-40 to 8-29-40, 30 mg. thiamin, daily, by hypo.; completed therapy without further nausea or vomiting; appetite improved
102. Mrs. P.R.	40	Cancer cervix uteri	7-29-40 to 8-24-40	6-10×15 (b)	10,200	Thiamin 9 mg.; liver; nausea slight during 4th week; appetite fair
103. Mrs. C.P.	60	Cancer left breast, postoperative	8- 6-40 to 9-11-40	1-10×15 1-15×15 1- 8×10 (e)	4,950	Thiamin 6 mg.; liver; nausea 0; appetite good
104. Mrs. J.F.D.	60	Cancer corpus uteri, with abdominal metastases	8- 8-40 to 9- 6-40	6-10×15 (b)	10,200	Thiamin 9 mg.; liver; nausea 0, up to 8-22-40, complained of slight nausea; 8-26-40, nausea moderate; thiamin increased to 18 mg., by hypo. once, then 9 mg. hypo., daily. No further nausea, and appetite improved
105. Mrs. E.K.	53	Tumor, left breast, preoperative	8-21-40 to 9- 9-40	3-10×15 (a)	3,600	Thiamin 9 mg.; liver; nausea 0; appetite good
106. Mrs. D.L.	48	Chromophobe adenoma of pituitary	9-16-40 to 10- 3-40	2- 8×10 2- 6× 8 (f)	3,200	Thiamin 0 at start; nausea severe after first week; thiamin, 9 mg. hypo., 9-24-40, then 9 mg. per os daily; nausea 0; appetite improved
107. Mrs. R.C.B.	48	Cancer cervix uteri and vagina	9-19-40 to 11- 4-40	6-10×15 (b) 1- 4 cm. (a)	10,200 4,800	Thiamin 9 mg.; liver; nausea 0; appetite improved
108. Mrs. H.W.C.	59	Cancer cervix uteri	9-19-40 to 10-17-40	6-10×15 (b)	10,200	Thiamin 9 mg.; liver; nausea 0; appetite very good

TABLE I—*Continued*

Case No. and Patient	Age	Diagnosis	Duration of Treatment	No. of Portals; Size in cm.*	Total Dosage in Roentgens†	Medication; Comments‡
109. Mr. J.E.C.	67	Cancer of bladder	9-23-40 to 10-26-40	3-10×10 1- 8×10 (f)	10,000	Thiamin 9 mg.; liver; nausea 0; appetite very good
110. Mrs. J.D.	52	Cancer cervix uteri	10- 1-40 to 10-28-40	6-10×15 (b)	10,000	Thiamin 9 mg. hypo. 1st day, then 9 mg.; liver; nausea 0 or slight(?); appetite good
		(Had severe nausea with vomiting during radium therapy-, without thiamin)				
111. Mrs. E.P.	53	Tumor, left breast, preoperative	10 4-40 to 10-17-40	3-10×15 (a)	3,600	Thiamin 9 mg.; nausea 0; appetite good
112. Mr. V.B.H.	52	Cancer prostate	10-10-40 to 11-19-40	1-10×12 2-10×10 1- 8×10 (f)	9,400	Thiamin 9 mg.; liver; nausea 0, appetite good
113. D.S. (F)	44	Cancer anterior thoracic wall, postoperative both breasts	10-11-40 to 10-31-40	2-15×20 (d)	3,600	Thiamin 9 mg.; nausea 0; appetite improved
114. Mrs. M.H.	79	Cancer of bladder	10-14-40 to 11-22-40	3-10×10 1- 8×10 (f)	8,500	Thiamin 9 mg.; liver; nausea 0; appetite improved
115. Mrs. H.F.A.	38	Cancer left breast, postoperative; sterilization	10-14-40 to 11-18-40	1-10×15 1-15×15 1- 8×10 2-15×15 (e)(c)	5,400 2,250	Thiamin 9 mg.; liver; nausea slight, one day after each pelvic treatment; appetite good
116. Miss E.S.	63	Cancer of bladder	10-14-40 to 11-20-40	3-10×10 1- 8×10 (f)	8,500	Thiamin 9 mg.; liver; nausea 0; appetite good
117. Mrs. K.D.	49	Endometrial hyperplasia	10-16-40 to 11- 8-40	2-10×10 1-15×15 (c)	3,300	Thiamin 9 mg.; nausea 0; appetite good
118. Mrs. W.H.B.	56	Cancer left breast	10-21-40 to 11-18-40	3-10×15 1- 8×10 (a)	7,200	Thiamin 9 mg.; liver; nausea 0; appetite good
119. Mrs. F.G.J.	58	Cancer left breast, postoperative	10-21-40 to 11-12-40	1-10×15 1-15×15 1- 8×10 (e)	5,400	Thiamin 9 mg.; nausea 0; appetite very good
120. Mrs. W.J.W.	32	Cancer of lungs metastatic from ovary	10-24-40 to 11-19-40	5-10×20 (c)	5,800	No thiamin at first; nausea in 2nd week; thiamin 9 mg.; nausea 0; appetite improved
121. Mrs. J.C.E.	50	Menorrhagia	10-30-40 to 11-19-40	2-15×15 (c)	1,800	Thiamin 9 mg.; nausea 0; appetite good
122. Mrs. L.S.	29	Endometrial hyperplasia	11- 2-40 to 11-19-40	2-15×15 (c)	1,800	Thiamin 9 mg.; nausea 0; appetite good

Schreiner and Stenström[16] advocated reducing the treatment time by increasing the power to the tube, active elimination before treatment, high intake of fluids and alkaline drinks, and 1,000 cc. of salt solution or 2 per cent solution of sodium bicarbonate per rectum after each treatment. In their report they state that with this regimen "unpleasant symptoms, with the exception of headache, nausea and vomiting, are rare."

Doub, Bolliger and Hartman[3,4] found other sedatives, especially codeine and luminal have been used rather widely and freely.

Young[17] reported good results with the use of liver extract, and referred to reports by Dietel and by Webster on the use of this preparation. Young gave an average daily dose of 2 cc. of liver extract, sometimes as much as 4 cc. daily; he reported 30 cases, with complete relief in 53 per cent, some benefit in 23 per cent, and no benefit in 23 per cent.

TABLE II

SUMMARY OF 122 CASES

Daily Amount of Thiamin Chloride	No. of Cases	Nausea 0	Nausea Slight	Nausea Moderate	Nausea Severe	Nausea, Vomiting Severe
Less than 6 mg.	6	0	2 (33%)	3 (50%)	1 (17%)	0
6 mg.	79	62 (78%)	14 (18%)	3 (4%)	0	0
9 mg.	46	36 (78%)	7 (16%)	2 (4%)	1 (2%)	0
Over 9 mg.	9	9 (100%)	0	0	0	0
Over 6 mg., totals	134*	107 (79.8%)	21 (15.7%)	5 (3.8%)	1 (0.7%)	0

* This table is a summary of 122 cases; 12 cases are listed in two groups, due to changes in dosage of thiamin during therapy.
Ninety-three of the 122 patients received concentrated liver extract, containing 6 mg. of thiamin chloride per cc., 0.5 cc. three times weekly; 35 of these patients also received calcium salts, 1 gram t.i.d.

that the administration of calcium reduced the acute sickness, also that morphine, glucose, and ether anesthesia relieved the symptoms.

Richards and Peters[15] used 1½ to 3 grains of nembutal given one hour before each treatment, or 2 grains of nembutal in suppositories. In their series of cases they found that 1 out of 40 would not tolerate barbiturates, and that 4 out of 40 developed resistance to the drug. They also gave diluted hydrochloric acid to combat the anorexia. Popp and Binger[14] also found pentobarbital sodium of value in reducing the incidence of nausea and vomiting, and

Martin and Moursund[10] observed that animals deprived of vitamin B_1 developed symptoms similar to those with roentgen intoxication; they found that animals given lethal doses of roentgen rays and then treated with vitamin B_1 survived or lived longer than the control animals. Their experiments suggested that vitamin B_1 gave some protection against roentgen intoxication.

Johnston[8] has recently reported that vitamin B_1 seems to be the medication which offers the most relief in roentgen sickness; in extreme cases she found that vitamin B_1 with small doses of nembutal gave satisfac-

tory results. Imler and Wammock[7] reported 21 cases treated with vitamin B_1, given hypodermatically, and state that roentgen sickness is controlled rapidly and effectively by the administration of vitamin B_1 in large doses.

The report of Martin and Moursund[10] suggested that the undesirable and unfavorable effects of irradiation might be minimized or relieved by the administration of vitamin B_1, which is a simple procedure and a not too expensive one if it would relieve the symptoms of irradiation sickness. This sickness, in its severe form, is not of very frequent occurrence, but is most likely to develop in those who are least able to withstand its effects, that is, in patients undergoing treatment for cancerous conditions. These patients are often poorly nourished, frequently anemic from blood loss, and often feeble from age and disease. It is in such cases that the rule, "treat the patient rather than the disease," must be followed, and frequently the treatment of the disease by radium or roentgen rays has been suspended or modified on account of the severe constitutional symptoms of irradiation sickness. Often, too, patients who were in good condition at the start of radiation treatment lost strength and weight, and became weak and feeble, after four or five weeks of roentgen treatments, with associated irradiation sickness; such patients required a prolonged convalescence to recover from the effects of radiation treatment. The sedative drugs, nembutal, luminal, codeine, and morphine, gave some relief but increased the anorexia, resulting in increased weakness and loss of weight. Frequently the fluid intake was so reduced that dehydration was a factor in increasing the debility.

Roentgen sickness of the severe type is not as frequent with the present methods of treatment with modern equipment as it was some years ago, but it is still far from uncommon. A very high percentage of patients undergoing radium or roentgen therapy experience mild symptoms, such as malaise and anorexia, which are accepted as a necessary part of the treatment. In any large series of therapy cases, between 10 and 20 per cent may be expected to develop more than mild symptoms of irradiation sickness, and without treatment most of these will have increasingly severe symptoms with continued irradiation.

Beginning in October, 1938, a series of patients undergoing treatment with 200 kv. roentgen rays were given thiamin chloride, synthetic vitamin B_1, in addition to other supportive and stimulative measures. These patients were all treated in the office, and their diets could not be supervised, but they were advised and encouraged to take a diet including liberal amounts of milk, eggs, fruits and fruit juices. Concentrated liver extract,[11] usually reticulogen, was given in 0.5 cc. doses, intramuscularly, three times weekly in more than two-thirds of the cases; calcium salts[3,4] were given to more than one-fourth of the cases, generally as the compound of calcium gluconate and dicalcium phosphate, 1 gram three times daily. Thiamin chloride was prescribed in 3 mg. tablets, each tablet equivalent to 1,000 international units of vitamin B_1; two tablets daily were ordered as the routine dose; if any nausea developed or the appetite was poor, this dosage was increased to three, four, or more tablets daily. Recently, the minimum dose was increased to three tablets, or 9 mg., daily, with additional amounts of thiamin as indicated. In most of the pelvic and abdominal cases, a pyramidal dose technique was used, starting with 100 r to each of two fields daily and increasing the amount of radiation each fourth day up to 500 r or more daily. This allowed time for the effect of the vitamin B_1 before the larger amounts of radiation were delivered.

This program of supportive treatment was not planned to test or prove the efficacy of vitamin B_1 therapy, but was started as an attempt to offset some of the unfavorable effects of roentgen therapy and to improve the condition of the patients during

the treatment period; for that reason, no control series of cases, without vitamin B_1 medication, was prepared.

The results have been most gratifying; in a series of 122 consecutive cases, in which roentgen irradiation was given to areas of the neck, thorax, abdomen, and pelvis, there was not one case of roentgen sickness of sufficient severity to require modification or suspension of the planned course of treatment; every case that developed nausea, or nausea and vomiting, was relieved or improved by increasing the dosage of vitamin B_1; in a few cases fairly large doses of thiamin chloride were given hypodermatically to relieve nausea. Many of the patients noticed an improvement in their appetites after a week or more of treatment; most of the patients improved in their general condition and sense of well being during the course of roentgen therapy, which was in marked contrast to our previous experience with patients undergoing similar courses of therapy. Sedatives and hypnotics were avoided, and were prescribed in only a few cases for pain or insomnia.

In some cases the value of thiamin was clearly demonstrated. Case 10, Mrs A. K. R., treated for cancer of the bladder, 11-29-38 to 12-27-38, developed severe nausea with vomiting; it was discovered that an error had been made in filling her prescription so that she was taking 0.3 mg. tablets instead of 3 mg. tablets; she was given 9 mg. of thiamin chloride, daily, per os, and after two days there was complete relief from nausea.

In Cases 12, 22, 80, 106, and 120, thiamin was not prescribed at the start of the roentgen treatments; in each case nausea developed after some days of treatment, and was relieved after administration of thiamin, usually in one or two days.

Case 81, a physician, did not take the full prescribed amount, 9 mg., of thiamin daily; in the third week of treatment he developed moderately severe nausea; he was given 0.5 cc. of concentrated liver extract containing 3 mg. of thiamin, intramuscularly, repeated three times weekly, and 9 mg. of thiamin chloride per os daily; his nausea was relieved and his appetite improved; he was able to continue at work and completed his treatments in very good condition.

Several cases developed slight or moderate nausea on a daily dosage of 6 mg. of thiamin; increasing the dose to 9 mg., or more, gave relief and generally improved the appetite; Case 96 required an increase to 15 mg. daily to relieve the nausea.

Case 49, Mrs. M. T., aged forty-eight, with recurrent cancer of the cervix uteri, had been treated in 1937 with 200 kv. roentgen rays; during the entire course of that treatment she had been nauseated, with some vomiting and no appetite, and was very weak at the completion of the course: she was treated from 9-14-39 to 10-18-39, through six 10×15 cm. portals, using roentgen rays generated at 200 kv., with 1.0 mm. copper and 1.0 mm. aluminum filters, pyramidal dosage, total of 10,200 r, measured in air; she was given 6 mg. of thiamin, daily, by mouth, and 0.5 cc. of reticulogen intramuscularly three times weekly; she did not develop any nausea, maintained a good appetite, and continued at work during the entire course of therapy.

Case 94, Mrs. J. L. W., aged fifty-eight, in 1938 was given roentgen treatments following a radical left mastectomy; she suffered from anorexia and nausea during the treatments, with loss of weight and strength. Following radical right mastectomy, roentgen treatments were given from 6-12-40 to 7-12-40, during which the patient was given 6 mg. of thiamin daily, and 0.5 cc. of reticulogen three times weekly; she had no nausea, maintained a good appetite, and gained several pounds in weight during the month of treatment.

Cases 70, 75, 82, 99, 102, and 110, had been severely nauseated during radium treatments preceding the roentgen treatments. During the period of the roentgen therapy, with thiamin administration, there was slight or no nausea.

Case 101, with abdominal metastasis from seminoma of the testis, developed se-

vere nausea and vomiting after eighteen days of treatment; he was given 60 mg. of thiamin, hypodermatically, then 30 mg. daily; the course of roentgen therapy was completed without further nausea, and with improvement in the patient's appetite.

SUMMARY

The literature of irradiation sickness has been reviewed, in part, and certain theories and methods of treatment abstracted from published reports. One hundred and twenty-two cases are reported, who were given thiamin, some of whom also received concentrated liver extract and calcium salts, during the period of roentgen therapy; these cases received treatment over fairly large areas of the neck, thorax, abdomen and pelvis (see Table 1). A considerable percentage of such cases would be expected to develop moderate to severe symptoms of roentgen sickness.

Any degree of nausea admitted or complained of by the patient was considered an indication of irradiation sickness; these cases were graded in four classes: slight nausea, moderate nausea, severe nausea with vomiting, and severe nausea and vomiting requiring modification of radiation therapy. Of the cases given 6 mg. or more of thiamin chloride daily, 79.8 per cent had no symptoms of irradiation sickness; 9 cases given more than 9 mg. of thiamin daily had no symptoms of irradiation illness. Table II shows the division of the cases according to the amount of thiamin given and the degree of symptoms of irradiation sickness.

CONCLUSIONS

The various theories as to the causes of roentgen sickness do not explain all of the clinical changes noted. None of the theories explain why a small dose of radiation over a moderate sized area of the body in certain individuals will cause rather marked constitutional symptoms, while larger doses in other cases cause no reaction nor any sign of irradiation sickness.

On the basis of the similarity of the symptoms of vitamin B_1 deficiency and those of irradiation sickness,[10] and the clinical results of vitamin B_1 administration in irradiation sickness,[7,8,10] it is suggested that vitamin B_1 is required to metabolize the products of nuclear disintegration or other substances produced in the body by irradiation, and that when there is an adequate supply of vitamin B_1 in the body irradiation sickness does not develop. It is known that vitamin B_1 is required for certain metabolic processes and that its effect is purely functional. In vitamin B_1 deficiency there is anorexia or decreased appetite, decreased tone of stomach and intestinal muscles with constipation, and certain types of nerve disturbances; in irradiation sickness, there is anorexia, nausea, vomiting and constipation.

Irritation sickness may be prevented by the administration of adequate amounts of thiamin chloride; from 6 to 9 mg. daily should be given to patients undergoing radium or roentgen therapy, and if any symptoms of irradiation sickness develop the amount of thiamin should be increased.*

I wish to express my appreciation to Dr. Clayton W. Eley for permission to use the cases on which this paper is based; these cases were all treated in the private service of Dr. Eley.

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* Continued use of thiamin during two more years has strengthened our conviction that administration of an adequate dosage of vitamin B_1 will prevent irradiation sickness.

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CLASSIFICATION OF EPITHELIAL CANCERS BASED UPON SITE OF ORIGIN*

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AN INCREASED responsibility is constantly being placed upon the radiologist in the diagnosis and treatment of malignant disease. More and more it becomes necessary to have a broader concept of cancer in general and, specifically, with respect to the individual manifestations.

By and large, prime importance has been placed upon the microscopic aspects of malignancy; but as we become more familiar with the effects of roentgen rays and radium upon the various tissues, we develop increased respect for the tumor bed and the particular region from which the malignant cells have their birth.

The recognition of these factors is highly important as a guide to the type of treatment to be used and the prognosis in the individual case.

Coutard,[1] in his various publications, has repeatedly stressed the importance of the tumor bed and pointed out the example of three lesions, i.e., those of the tonsil, the anterior pillar and the posterior pillar, wherein are presented three different types of malignancy all having their origin within a few millimeters of each other and all capable of enveloping the other in their growth. Each of these manifests a sensitivity that is inherent in its tissue of origin and largely independent of the individual cell type.

Roux-Berger[2] demonstrated that the curability of various lingual lesions depended greatly upon the particular portion of the tongue which was involved.

Cutler, Buschke and Cantril[3] have indexed the subject matter with considerable emphasis upon this concept of tumor origin.

The matter has been brought to our attention more profoundly during the past year when it was decided to review some two thousand cases of cancer which had been treated since 1932 in our own institution. The review was undertaken with a two-fold purpose, namely, to evaluate the results of treatment and at the same time to reclassify the cases so that a more satisfactory cross-index could be instituted and promulgated.

It would seem almost imperative that various workers in this field have a common classification if we are to compare the results of various techniques and methods of treatment.

Lastly, we find it most stimulating to adhere to a rigid classification of this type. An exhaustive study from the standpoint of history, physical examination, roentgen examination and microscopic study is often necessary to accomplish this purpose. The net result in knowledge gained of each particular lesion is well worth the effort.

The proposed classification embraces only the epithelial malignancies with the sole exception of the lymphosarcomas, many of which originate in and about Waldeyer's ring. These are included on the basis of behavior simulating that of the carcinomas.

The numerical listings included in the following classification serve no purpose other than to indicate the relative proportions in which the various lesions have presented themselves in our own series of cases treated between 1933 and 1940 inclusive.

SUPERFICIAL EPITHELIOMAS

Superficial cancers of the face, neck, and scalp constitute by far the greatest percentage of malignant lesions treated by the radiologist. We classify many of these as originating in special localization, such as

* From the radiological clinic of Drs. Groover, Christie, and Merritt. Presented at the Forty-second Annual Meeting, American Roentgen Ray Society, Cincinnati, Ohio, Sept. 23–26, 1941.

	Cases
1. Face, neck and scalp	523
a. External ear	55
b. External auditory canal	3
c. Eyelid	33
d. Ocular conjunctiva	0
e. Nose	89
f. Lip	103
g. Other lesions of this region without a special tumor bed	240
2. Extremities	37
3. Trunk	11
4. Penis	5
5. Vulva	16
6. Anus	7

upon a cartilaginous base, because they constitute certain problems both as regards treatment and prognosis. Consider, for instance, a carcinoma of the external auditory canal as compared with an epithelioma of the lip, both of which are relatively of very superficial origin, yet the former is rarely curable whereas the latter is just the opposite.

In most discussions of malignancy, epitheliomas of the penis are included with the male generative organs, while those of the vulva are included with the female generative organs. It would seem that their superficial origin demands that they more rightly be placed in the category of superficial epithelioma of special location. The same holds for carcinoma of the anus which usually is included with carcinoma of the alimentary tract; but the picture is that of superficial epidermoid carcinoma and the mere fact that they tend to infiltrate past the mucocutaneous junction into the rectum before they are usually recognized clinically makes them no more a portion of the alimentary tract than does an epithelioma of the lip extending into the mouth make it a carcinoma of the buccal cavity.

NASAL CAVITY

	Cases
1. Turbinates	3
2. Septum	4

It is sometimes difficult to differentiate precisely the site of origin of these lesions. In the first place, there are a relatively small percentage of lesions that originate within this region. One must be careful to differentiate epitheliomas originating in the nasal accessory sinuses, particularly the ethmoids or the antra and invading the nasal fossa secondarily, from primary lesions in this region. It is also sometimes difficult to determine whether lesions which fill the choanae actually originate within the nasal cavity or within the nasopharynx.

NASAL ACCESSORY SINUSES

	Cases
1. Sphenoids	0
2. Frontals	2
3. Ethmoids	3
4. Antra	16

Primary epitheliomas of the sphenoids must be exceptionally rare. Most malignant lesions in this region must originate in the nasopharynx and invade the sphenoid sinus secondarily. Likewise, epitheliomas of the frontal and ethmoid sinuses are seldom seen.

The antra are by far the most common site of malignant degeneration in the nasal accessory sinuses. They often grow to quite large size and may invade either the orbit or the nasal fossa, or the hard palate and superior alveolus before they are recognized clinically. These facts must always be borne in mind when lesions presenting in these locations are submitted for diagnosis and treatment.

ORAL CAVITY

	Cases
1. Alveolus	25
2. Buccal mucosa	26
3. Hard palate	1
4. Tongue	62
a. Dorsum	26
b. Base	14
c. Infralingual portion	22

The infralingual portion of the tongue includes those lesions of the floor of the mouth. At times it is difficult to determine whether a lesion arises on the epiglottis or in the base of the tongue. As stated above, it is also imperative when confronted with a lesion of the hard palate or superior alveolus to eliminate the antrum as a primary site of origin. Dorsal lingual lesions present

an entirely different problem from those of the base of the tongue or infralingual lesions due largely to the dense vasculo-connective tissue constituting the tumor bed.

NASOPHARYNX

1. Roof
2. Posterior wall
3. Lateral wall

Total ..... 15 cases

Lesions of the nasopharynx have usually grown to such a large extent before they are recognized that a precise appraisal of their site of origin is extremely difficult. It would appear, however, that there are at least three definite locations from which these originate. Undoubtedly, some of these lesions must begin in the eustachian tubes although this is extremely difficult to prove.

OROPHARYNX

	Cases
1. Anterior pillar	2
2. Tonsil	34
3. Posterior pillar	1
4. Soft palate	9
5. Free border of the epiglottis	4

Lesions of the tonsil, as is well known, are extremely sensitive and offer an excellent prognosis if found without glands, whereas lesions of the anterior pillar are exactly opposite and are seldom, if ever, curable. Lesions of the soft palate and free border of the epiglottis are quite sensitive to radiation; also, with the latter type, quite prone to exhibit glands, when first seen.

Lesions of the posterior pillar, while exhibiting a moderate degree of sensitivity, are often accompanied by extensive invasion in the lateral and posterior pharyngeal walls.

HYPOPHARYNX

	Cases
1. Lateral pharyngeal wall	4
2. Posterior pharyngeal wall	3
3. Pyriform sinus	9
4. Aryepiglottic fold	1

The close proximity of the hypopharynx and the larynx has led to considerable confusion regarding lesions originating within this region. The otolaryngologist classes many of these as intrinsic and extrinsic carcinoma of the larynx based upon extent of the disease. This is entirely a surgical concept and disregards the fact that a lesion originating within the hypopharynx and involving the larynx secondarily is an entirely different matter from a lesion originating within the larynx involving secondarily the hypophyarynx. A history of hoarseness and dysphagia characterizes malignancies of these sites, and the sequence of development of these two symptoms when both exist is almost a certain clue as to the site of origin.

Hypopharyngeal lesions do not manifest the curability that laryngeal lesions do. Lesions of the posterior pharyngeal wall, while they often manifest a primary sensitivity, tend to infiltrate far upward and downward under the mucosa and are rarely, if ever, sterilized. The same holds for lesions of the lateral pharyngeal wall. Lesions of the pyriform sinus seem to be controlled in a small minority of cases but invasion or recurrence in the constrictor muscles of the esophageal mouth is extremely common and prevents a cure. Lesions of the aryepiglottic fold are at the dividing line between the pharynx and the larynx and are usually either laryngeal or pharyngeal. We have had one lesion originating high up on the free border of the aryepiglottic fold near the point of insertion with the epiglottis that was extremely sensitive.

LARYNX

	Cases
1. Vestibule	12
2. True cord	11
3. Subglottis	2

Vestibular lesions include those epitheliomas originating on the laryngeal face of the epiglottis, the false cord and the ventricular cavity, and manifest a high degree of radiosensitivity and radiocurability when they have not invaded too far. They are prone to earlier glandular involvement than are lesions of the true cord or subglottis, and in this respect they partake very much of the character of hypopharyngeal lesions. It would appear that vestibular lesions are,

for the most part, inoperable even by the most ambitious surgeon.

Lesions of the true cord are most certainly radiosensitive and radiocurable in a large percentage of cases unless they assume primary infiltrative characteristics, as noted by early and complete fixation with or without involvement of the cartilages. Lesions of the subglottis are the most uncommon and must be differentiated from primary lesions of the trachea. The close proximity to the cricoid cartilage with tendency toward infiltration in many instances leads to a poorer prognosis from the standpoint of radiotherapy.

TRACHEA

Total number of cases	3

Carcinoma of the trachea, as one gleans from the literature, must be extremely unusual. We have treated 3 cases in the past eight years, one of which was treated in 1934 and lived without a recurrence until one year ago. The other two have been treated in the last two years and both have been dramatic in their response to irradiation, and remain symptom free to date.

LUNG

Total number of cases	28

We can dismiss this without going further. It seems to be the general consensus that all epitheliomas of the lung are of bronchogenic origin.

ALIMENTARY TRACT

	Cases
1. Esophagus	12
2. Stomach	55
3. Small bowel	0
4. Large intestine	46
5. Rectum	69

Epitheliomas of the large intestine include the rectum from a strictly anatomical standpoint. Its special location, however, with ready accessibility from the anal orifice justifies a separate classification.

LIVER, BILIARY PASSAGES, AND PANCREAS

It is extremely difficult to differentiate the various sites of origin of cancers in this region. Carcinomas of the head of the pancreas and biliary passages are often such an integral part of the entire malignant process discovered either at operation or autopsy that much study is necessary to arrive at a precise diagnosis.

1. Liver	
2. Bile ducts	
3. Gallbladder	
4. Head of the pancreas	
5. Tail of the pancreas	
Total number of cases	11

FEMALE GENERATIVE ORGANS

	Cases
1. Ovary	65
2. Corpus uteri	67
3. Cervix uteri	331
4. Vaginal walls	12

Little need be said regarding carcinoma of the ovary. The diagnosis is usually made at operation and the sensitivity and prognosis will probably ultimately depend upon its degree of dissemination, and second, whether it is a solid or cystic type of tumor, and if solid, the microscopic site of origin as determined by cellular characteristics.

Carcinoma of the corpus uteri must be differentiated from cancer of the cervix, however, and regarding this we have only two things to say: Undoubtedly, we may find an adenocarcinoma of the cervix but it is extremely rare to be presented with an epidermoid carcinoma originating within the corpus; the endocervical origin of many epidermoid carcinomas must always be kept in mind and may exist without visible evidence of ulceration. The differentiation from corpus cancer must be made from the histologic picture.

Regarding epitheliomas of the vaginal walls, as one studies them more carefully they fall into a very small minority and usually represent upward extension from carcinoma of the vulva or downward extension from carcinoma of the cervix.

MALE GENERATIVE ORGANS

	Cases
1. Prostate	59
2. Testicle	20

URINARY TRACT

	Cases
1. Kidney	31
2. Bladder	80
3. Urethra	5

ENDOCRINE GLANDS

	Cases
1. Thyroid	8
2. Parathyroid	1

BREAST

Total number ..... 574 cases

SUMMARY

It is obvious that there are imperfections and difficulties in formulating and applying a classification of this type. Theoretically, and practically, other sites of origin for epitheliomas must exist, as for instance, the lacrimal glands, fallopian tubes, vas deferens, etc. Yet we find that grouped in this classification are embraced the vast majority of all cancers which come to the radiologist for diagnosis and treatment. A cross-index file based upon this classification makes cases readily accessible to follow-up and study. The concept is purely anatomical and is largely divorced from previous surgical or pathologic and microscopic impressions.

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DISCUSSION

Dr. Howard P. Doub, Detroit, Mich. This is a very interesting paper, essentially on the anatomical classification of malignant tumors, without taking into account the pathological cell structure. The regional origin of these tumors connotes to radiologists certain clinical impressions which we have gained over a period of years, and this has been indicated in several instances by the authors. We feel, however, that the pathological classification based on histological sections is also of importance, and has important implications, as it indicates to us in many instances the radiosensitivity of tumors, the probability of metastases, the rate of growth of the tumor, and certain reactions of fibrous tissue.

To radiologists the regional origin of tumors, of course, indicates rather broadly certain clues as to cell type. If the tumor involves the lower lip, it is usually of squamous cell origin, whereas in other portions of the face it may be of either type, but is usually basal cell in type.

It would have been interesting for Dr. Caulk to give us the type of radiotherapy which he used, either the fractionated type of therapy or the massive dose, the amount of voltage, the number of roentgens, and so forth.

We feel that the tumor bed is an extremely important factor in our treatment of tumors, in our estimation beforehand, how much dosage can be safely applied, and what the results are likely to be. In many instances, of course, these tumors are not available to direct irradiation and therefore we are handicapped to start with. Some of these tumors that he showed here on the anterior pillar could be treated more advantageously and with better results if they were available to direct irradiation, such as the squamous cell tumors that occur on the lower lip. We are, of course, limited by the vital structures around the tumor so that we cannot always apply the dose that we wish, and in some instances we cannot apply it at right angles. We attempt, of course, with small limiting tubes,to get the radiation in and to shield the surrounding structures but, as we all know, that is a very difficult procedure in many cases.

I think the authors are correct in calling tumors in various parts of the body epitheliomas. You can broadly use an anatomical and a pathological description, and, by combining those two, can obtain a better classification.

THE EFFECT OF ROENTGEN IRRADIATION ON EPIPHYSEAL GROWTH

I. EXPERIMENTAL STUDIES UPON THE ALBINO RAT*

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IN THE course of an earlier investigation[6] it was shown that the growing epiphyseal plate of the albino rat was very markedly sensitive to roentgen irradiation. It was noted that relatively small doses caused sufficient injury to interfere significantly with the growth process. The apparent specificity of this effect upon epiphyseal cartilage with smaller doses (600–1,800 r) and the absence of associated permanent injury in other structures within the field of treatment (bone, skin and bone marrow) was considered noteworthy.

The present investigation was undertaken to amplify this study and to determine the following points:

1. What dosage produces maximal effect on the epiphyseal plate without permanently damaging juxta-epiphyseal tissues?
2. What is the effect of varying dosages on longitudinal bone growth?
3. Does bone deformity, maldevelopment, or fragility occur after such treatment?

To this end, graded dosages of roentgen rays were applied to the growing epiphyses of albino rats and a series of roentgenographic and histologic studies pursued.

METHODS

One hundred and thirty-three albino rats of the same stock constituted the experimental group. These were subdivided according to age at the time of irradiation into Group I, in which the animals were thirty days old; Group II, ninety days old; and Group III, 180 days old. The purpose of this division was to determine the variability of response, if any, which might result from differences in growth rate at varying ages.

The rats in Group III, 180 days old, had relatively mature skeletons and grew so slowly during the period of observation that accurate measurement of change in bone length was impossible. This group was therefore excluded from final roentgenographic consideration.

All animals were housed in suspended open meshed wire cages and subsisted upon the Sherman BMS diet recommended by Russell.[11] To this, there was added for the purpose of incidental studies 3 per cent by weight of Dutch madder.[1]

Each group contained 3 control animals to whom no radiation was administered. These served merely as direct check controls since considerable material was available from untreated extremities in the treated animals. The age groups were subdivided into treatment groups in each of which were approximately 6 animals. All of the animals in a given treatment group received equal amounts of radiation, the individual group dosages ranging as follows: 665 r, 835 r, 1,000 r, 1,165 r, 1,335 r, 1,500 r and 1,800 r. Each dose was administered at a single sitting to the right hind extremity, the field centering about the knee joint. The apparatus was so arranged that the medial surface of the thigh received the entrance dose and the lateral aspect, the exit dose. The remainder of the body was adequately protected by a lead screen.

Roentgens were measured in air with a Victoreen dosimeter and were derived from a Picker-Waite generator, the qualities of which were as follows: 200 kv. (peak), 20 ma., 24 cm. distance, 0.25 mm. copper plus 1.0 mm. aluminum filtration, intensity 203 r per minute, copper half-value layer 0.75 mm.

Animals were immobilized for irradiation by strapping with adhesive tape and an Ace band-

* Aided by a grant from the National Foundation for Infantile Paralysis, Inc.

age to a Y-shaped plywood board, the hind extremities being abducted upon the divergent arms of the Y. Teleroentgenograms were taken within a few days before irradiation and again upon the day on which the animals were sacrificed. The rats were sacrificed by decapitation at intervals ranging from one to thirty-six weeks after irradiation, the schedule being so arranged that a period of four to six weeks usually intervened between the sacrifice of subjects from the same treatment groups.

Material for histologic study was chosen as follows:

(*a*) Two sections of skin within the area traversed by the roentgen-ray beam, one from the lateral and one from the medial aspect of the lower end of the thigh. The lateral specimen included subcutaneous tissue and both superficial and deep musculature, the medial extended through the fatty panniculus only. In a few instances lymph nodes were included.

(*b*) The knee joint was then exposed and a fragment of infrapatellar synovia excised.

(*c*) The femur was disarticulated, freed of investing soft tissues, and the lower one-half split longitudinally between the condyles. Sections thus included metaphyseal bone, epiphyseal plate, epiphysis and articular surface.

(*d*) From the metaphyseal end of the femoral shaft a portion of marrow was removed with a blunt probe and deposited upon a small piece of filter paper.

Soft tissues were all fixed in Zenker's fluid with acetic acid and paraffin sections were stained with phloxine-methylene blue. Bone was fixed in Bouin's solution, decalcified with 5 per cent nitric acid in alcohol, and stained with hematoxylin-eosin.

Sections from each of the aforementioned areas were studied in order to establish the presence, if any, of injurious effects of irradiation and to grade these according to the degree of severity of the lesion. Since detailed histologic data have been described elsewhere,[6,7,9] the observations are recorded in comparatively brief form. Attention was directed primarily at the determination of that amount of roentgen irradiation which would effectively impede activity of the epiphyseal plate but would not interfere with the integrity of adjacent or covering structures.

OBSERVATIONS

Skin and Subcutaneous Tissue. With the amount of irradiation utilized in these experiments only minimal cutaneous reactions are produced. No evidence of permanent alteration of structure is elicited. Doses up to 1,165 r cause only slight vascular congestion (one to four weeks), minor degrees of keratosis (three to six weeks), and scanty infiltration of the corium with small numbers of lymphocytes and monocytes (one to four weeks). With 1,335 r or more these lesions are increased slightly in prominence and in addition an occasional hair follicle exhibits loss of sheath stratification, epithelial degeneration and epilation (two to five weeks). These changes never attain significant proportions and after the tenth to fourteenth week no residual abnormality can be detected. Subcutaneous tissue, blood vessels, sebaceous glands and skeletal muscle remain unaffected. In lymph nodes included in these sections a few show excessive numbers of phagocytic cells within their sinuses, but they are otherwise not remarkable.

Sections taken from the medial aspect of the thigh are histologically identical with those from the outer side with dosages of 1,165 r or less. Larger amounts of irradiation cause a slightly greater degree of round cell infiltration and hair follicle degeneration on the inner surface of the thigh (the area directly subjected to the roentgen rays). Such lesions are focal, however, and subsequent epilation is never sufficient to permit microscopic recognition. Small clusters of lymphocytes and a few stunted hair follicles persist up to twenty-two to thirty weeks after irradiation but after this period complete re-establishment of the normal structure occurs. Sweat glands, present only on the inner surface of the thigh, are apparently unaffected by the doses applied.

Bone Marrow. The results of the present study are in complete agreement with the observations made upon the series studied in our earlier investigations.[9] There is depletion of approximately one-half or less of the marrow cellular content in the field of irradiation within two to three weeks (Fig. 1). There are no indications of actual necro-

sis; expansion of fat replaces the cells which have disappeared. Regeneration during the

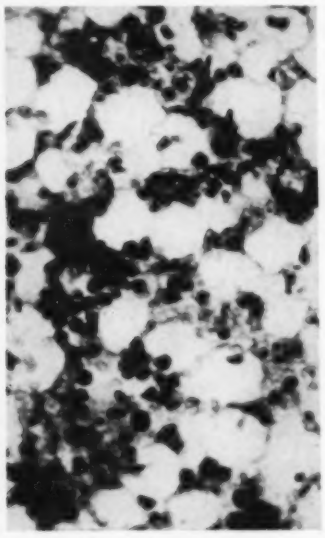

FIG. 1. Femoral bone marrow ten days after irradiation (1,000 r). There is marked depletion of marrow cells with replacement of fat. There is no evidence of necrosis. ×350.

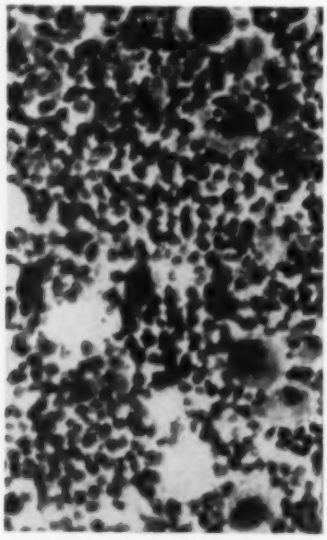

FIG. 2. Femoral bone marrow thirty-five days after irradiation (1,165 r). Marrow cellularity has returned to a level approximating the normal. Few fat vacuoles are evident, and in this area there are 5 megakaryocytes. ×350.

succeeding two to four week period permits the return of cellular volume to a level approximating that preceding treatment (Fig. 2). With dosages up to 1,335 r this constitutes the complete sequence of events. Higher dosages cause a secondary fall which, however, with the amount of irradiation applied in these studies rarely exceeds that of the primary phase. A dosage of 1,500 r causes a permanent reduction to approximately two-thirds of the normal, but higher doses are followed by more marked hypocellularity, hematopoietic elements comprising only one-half to one-fourth of the pretreatment marrow content (Fig. 3). These changes necessarily indicate evidence of significant injury but it should

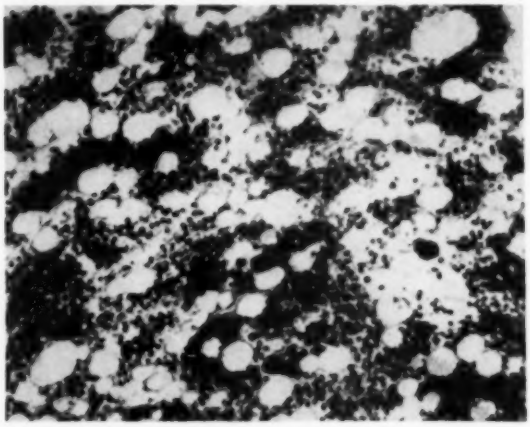

FIG. 3. Femoral bone marrow 190 days after irradiation (1,800 r). Marrow has again been diminished in cellularity and the fat content proportionately increased. ×150.

be remarked that such alterations have been observed only in the highest dose group.

Observations of qualitative effects may be summarized briefly. Primary diminution of marrow content is almost wholly the result of a sharp fall in the number of normoblasts, elements constituting approximately one-half of the nucleated components of normal marrow. Apparent regeneration of these cells contributes to the re-establishment of marrow bulk during the second to fourth week following dosages of 665 to 1,165 r. Animals subjected to greater amounts of irradiation reveal very slight normoblastic regeneration, the secondary rise resulting mainly from an absolute in-

crease in the number of polymorphonuclears. In these rats, subsequent to the attainment of the peak of regeneration, the relative numbers of nucleated red cells continue to diminish progressively, so that in later specimens, mature granulocytes constitute the great majority of marrow cells.

Despite the variation in cell content there is no evidence of abnormality of the fatty marrow (Fig. 3). This tissue merely exhibits a compensatory increase during the periods of hypocellularity. Neither fibrosis, edema, hemosiderosis, nor blood vessel abnormality is detected. It is reasonable to conclude, therefore, that with the exception of blood forming cells no significant injury is sustained by any of the mesenchymal and nutritional elements comprising the marrow

Synovia. The synovia in the region studied normally consists of fibrofatty tissue with only moderate vascularization. Overlying this stroma synovial cells are sparse and flattened in appearance. A rare phagocytic cell is observed in the subsynovial tissue.

Irradiation with 1,165 r or less causes no detectable variation from the normal. Dosages of 1,335 and 1,500 r apparently cause focal thickening of the synovial layer without particular evidence of intrinsic damage. In such regions synovial cells are somewhat more cuboidal in shape and very occasionally form two or three superimposed layers. Monocytes and lymphoid cells are slightly increased in numbers in the subsynovial region but are never very abundant. No evidence of necrosis or unusual proliferative activity is noted (Fig. 4). With 1,800 r single clusters of monocytes assuming the appearance of epithelioid cells are observed in a few specimens. These are never associated with the faintest suggestion of caseation or giant cell formation.

The Epiphyseal Plate. The data recorded by Dawson[3] and our own control series have shown that epiphyseal plate activity in rats in both proximal tibia and distal femur is continuous throughout the entire age period studied in this investigation. Maximal ages attained in the youngest and oldest groups were 300 and 450 days respectively. It was found, however, that the rate of growth could not be predicted on

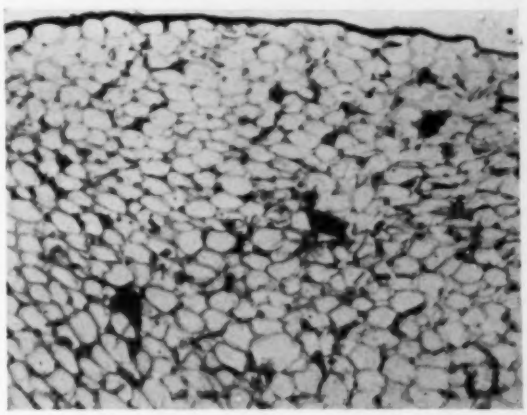

Fig. 4. Infrapatellar fat pad 100 days after irradiation (1,800 r). The synovial surface is intact and the subsynovial fat normal in appearance. ×140.

the basis of the morphologic structure alone. In older animals the cartilage of the epiphyseal plate proper was histologically indistinguishable from that found in the youngest rats. In spite of this the rate of growth was found by roentgenographic studies to diminish slowly up to the nineteenth to twenty-fifth week of life and at this point to exhibit a sharp drop in rate. As a result the increase in length of the tibia in the ninety day old control group was considerably less than in the thirty day old rats over a given period and the rate of growth in the 180 day animals so slow that roentgenographic measurements of length increment were made with difficulty.

In appreciating histologic lesions the morphologic criteria for the normal rat epiphysis as described by Dodds and Cameron[4] have been adopted (Fig. 5). Earlier observations were confirmed and it was noted that the extent of cartilaginous alteration was roughly proportionate to the amount of irradiation administered.

Evidences of injury became apparent within a week after irradiation. These are moderately severe after 665 r and very severe with higher doses, although the

degree mounts progressively with the intensity of treatment. Lesser changes are exemplified by swelling of the chondrocytes,

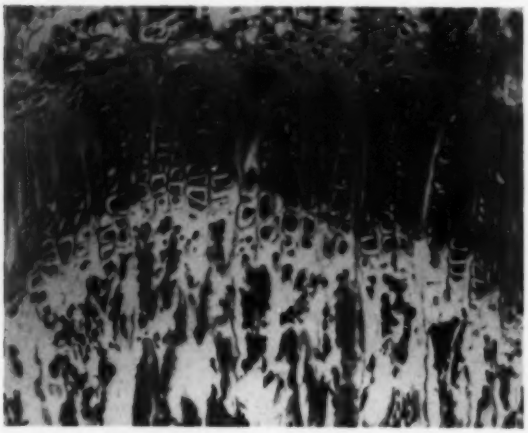

FIG. 5. Lower femoral epiphyseal plate in a normal, untreated, thirty day old rat. Regular columns of active chondrocytes are arranged parallel with the long axis of the bone. Deposits of new bone may be seen along the lowermost portions of the cartilaginous trabeculae. ×150.

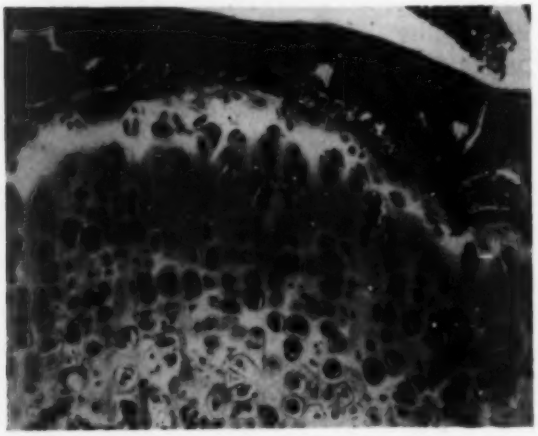

FIG. 6. Epiphyseal plate fourteen days after irradiation (1,165 r). Although the columnar structure persists, the columns are irregular and component chondrocytes are swollen and in many instances pyknotic. Cartilage matrix is mottled in appearance. ×150.

irregularity of columns and variation in staining power of the matrix (Fig. 6). Rats receiving 835 to 1,165 r exhibit progressive disruption of chondrocytic columns, mottling of the matrix and vacant lacunae. Interference with growth is manifested by stunting and ultimate disappearance of primary calcified trabeculae and the development of a subepiphyseal osseous plate (Fig. 7). The latter presumably results from the continued function of apparently unaffected osteoblasts in the absence of the calcified cartilage framework ordinarily available.

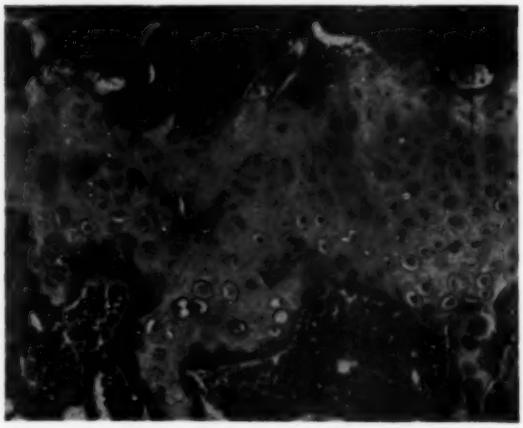

FIG. 7. Epiphyseal plate 184 days after irradiation (1,165 r). Columnar arrangement is completely disrupted and cartilage cells are swollen and varied in size. A thin plate of bone has been deposited along the metaphyseal margin of the epiphysis and calcified cartilaginous trabeculae are no longer evident. ×140.

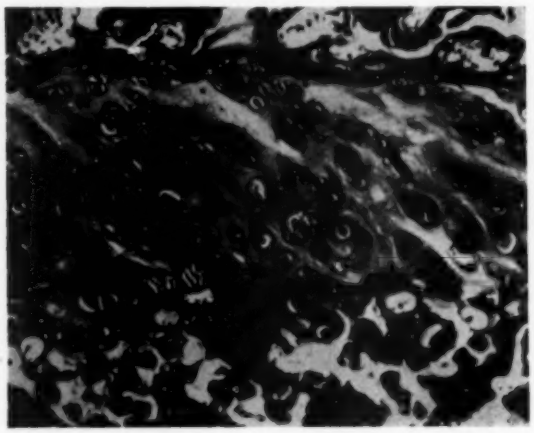

FIG. 8. Severely damaged epiphyseal plate seventy-six days after irradiation (1,800 r). Chondrocytes are disarranged and obviously degenerated. The matrix is frayed and crumbly in appearance. A dark staining layer of subepiphyseal bone may be noted. ×140.

Submaximal to maximal lesions are evident with dosages of 1,335 to 1,800 r and the degree of injury is considerably greater in these groups than in the 665 to 1,165 r range. The epiphyseal cartilage plate is crumbled in appearance, markedly irregular in thickness, and in a few instances, narrow, bony strands pierce the matrix joining the epiphyseal with the metaphyseal plates. These changes unquestionably prevent any significant contribution on the part of the cartilage to further bone growth (Fig. 8).

From the histologic aspect the character of the lesion produced is the same in all age groups.

Evidence of re-establishment of normal histologic structure in even the minimally deranged cartilage is not elicited. In a few instances as might be expected more commonly among the youngest animals, rather scanty apparent reactivation of cartilage cells occurs. This phenomenon, rarely appearing before the sixtieth post-treatment day, is manifested by the development of circumscribed clusters of viable chondrocytes which are normal in appearance but not in distribution. These are aggregated into spherical masses surrounded by thin zones of deeply basophilic matrix. The masses never exceed the size of a single high power field and lack normal orientation to the long axis of the bone. For these reasons they would seem incapable of contributing to the longitudinal growth process and their rarity precludes the development of recognizable deformity. In rare instances such reactivation is associated with a certain degree of orientation. Short columns of cartilage cells are observed growing parallel with the long axis of the shaft. Between the columns is a variable amount of normal matrix. Growth in these foci evidently permits their separation from the degenerated cartilage and sclerotic subchondral plate but the amount of displacement is never of significant extent.

Except for the bony plate formed in the region ordinarily occupied by primary calcified trabeculae no apparent variation from the normal occurs in osseous tissue. Cortical bone retains its usual thickness and compactness in the areas treated and since no deformity developed it is reasonable to assume that its durability is unaffected. Endosteum, periosteum and submetaphyseal trabeculae retain their histological integrity.

Articular Cartilage. By comparison with the epiphyseal plate, articular cartilage exhibits a considerable degree of immunity to roentgen irradiation. Despite the presence of profound disarrangement in the cartilage of the epiphyseal plate, articular surfaces in the immediate vicinity and unquestionably in the path of the roentegn beam are perfectly smooth, obviously functionally unimpaired and show minor intrinsic lesions which are readily matched in control joints (Fig. 9). The length of the experiments was sufficient to permit the development of degenerative joint processes secondary to the altered state of the epiphysis. However, in order to exclude with certainty the possibility of such sequelae further studies relating to the effect of greater weight bearing and activity in such treated joints are in progress.[2]

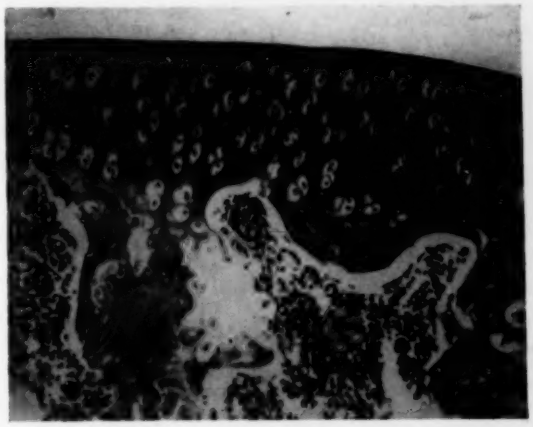

Fig. 9. Femoral articular cartilage seventy-six days after irradiation (1,800 r). Despite severe degenerative changes caused by this dosage in cartilage of the epiphyseal plate, the articular surface is smooth, the chondrocytes visible, and the matrix homogeneous in structure. ×140.

Roentgen Findings. Teleroentgenograms of both lower extremities before treatment

and at varying intervals thereafter show no appreciable change in the architecture of the treated bones following dosages up to 1,165 r. Those tibiae and femora receiving treatment in excess of 1,165 r, however, frequently show a zone of increased density in the metaphyseal region with definite local irregularity of the trabecular structure (Fig. 10).

FIG. 10. Roentgenogram of the irradiated and unirradiated legs of the rats sixteen weeks after a single dose of 1,200 r. Note the difference in length of the tibiae and the zones of increased calcium deposit about the epiphyseal lines of the irradiated knee.

Fracture occurred in only one instance. This was found to be in the mid-shaft in an area which was not exposed to irradiation and could be explained adequately by trauma sustained in the handling of the animal. It was believed that the irradiation had nothing to do with its occurrence.

DISCUSSION

This investigation was motivated initially by the possibility of a practical use for the known radiosensitivity of the epiphyseal plate. Shortening of as much as 4 inches may occur in a leg paralyzed by anterior poliomyelitis. If the treatment of the shortening is delayed until full growth is attained it is necessary to resort to leg lengthening or leg shortening operations. During the period of active growth it is possible to cause premature arrest of epiphyseal growth by epiphyseodesis (Phemister[10]). This procedure carries with it some risk of wound infection, induced deformity and other surgical complications.

The substitution of roentgen irradiation as a means of limitation of the growth of an unaffected limb might conceivably offer advantages (Judy[8]). It would be necessary, however, to demonstrate that no permanent injury would be produced in juxtaepiphyseal structures; that dosages might be so minimized that bone deformity, maldevelopment or fragility would not result; and that a reasonably constant interference with normal growth from the epiphyseal plate could be established.

Interest in this study has therefore been directed fundamentally at these features and accordingly it was shown that treatment with 1,165 to 1,335 r of roentgen rays at 200 kv. was sufficient to cause major interference with epiphyseal activity in the albino rat. Doses between 665 and 1,165 r caused significant but less marked retardation of longitudinal growth.

Measurements of the treated and untreated tibiae before and at various intervals after irradiation demonstrated a definite retardation in growth of the treated bone as compared with the normal growth of the untreated tibia of the opposite leg. Since the activity of the upper tibial epiphyseal plate paralleled that of the lower femoral region[3] and since this bone was more readily susceptible to accurate roentgenography than the femur, it was believed advisable to use it for measurement rather than the femur from which histologic studies were made. Even the lowest dosage used, namely 665 r, was effective in producing definite growth retardation (Tables I and II). The amount of retardation (calcu-

TABLE I

MEASUREMENTS OF TIBIAE FOLLOWING IRRADIATION OF THIRTY DAY OLD RATS

Dosage in Roentgens	Duration of Experiments in Weeks	Untreated Tibiae, Length in cm.		Treated Tibiae, Length in cm.		Length Increment in cm.			Percentage Retardation c/a
		Before	After	Before	After	Untreated a	Treated b	Difference c	
865	10	2.5	3.3	2.5	3.2	0.8	0.7	0.1	12.5
	16	2.3	3.5	2.3	3.3	1.2	1.0	0.2	16.6
	23	2.3	3.7	2.3	3.4	1.4	1.1	0.3	21.5
	29	2.5	4.2	2.5	3.9	1.7	1.4	0.3	17.6
835	7	2.6	3.6	2.6	3.4	1.0	0.8	0.2	20.0
	13	2.7	3.9	2.7	3.7	1.2	1.0	0.2	16.6
	26	2.6	4.0	2.6	3.6	1.4	1.0	0.4	28.5
	32	2.5	3.7	2.5	3.3	1.2	0.8	0.4	33.3
	36	2.5	4.1	2.5	3.8	1.6	1.3	0.3	18.7
1000	8	2.3	3.2	2.3	2.9	0.9	0.6	0.3	33.3
	10	2.5	3.8	2.5	3.2	1.3	0.7	0.5	38.4
	16	2.4	4.1	2.4	3.6	1.7	1.2	0.5	29.4
	22	2.4	4.0	2.4	3.6	1.6	1.2	0.4	25.0
	29	2.6	4.2	2.6	3.6	1.6	1.0	0.6	37.5
	35	2.5	4.1	2.5	3.5	1.6	1.0	0.6	37.5
1165	1	2.7	2.7	2.7	2.7	0.0	0.0	0.0	0.0
	7	2.5	3.2	2.5	3.0	0.7	0.5	0.2	28.5
	13	2.6	3.9	2.6	3.2	1.3	0.6	0.7	53.8
	15	2.4	3.6	2.4	3.1	1.2	0.7	0.5	41.7
	19	2.6	3.9	2.6	3.3	1.3	0.7	0.6	46.2
	32	2.6	4.0	2.6	3.3	1.4	0.7	0.7	50.0
1335	3	2.4	2.8	2.4	2.8	0.4	0.4	0.0	0.0
	16	2.6	3.9	2.6	3.8	1.3	1.2	0.1	7.7
	19	3.2	4.0	3.2	3.5	0.8	0.3	0.5	62.5
	28	2.3	3.9	2.5	3.9	1.4	1.4	0.0	0.0*
1500	3	2.5	2.6	2.5	2.6	0.1	0.1	0.0	0.0
	7	2.7	3.3	2.7	3.0	0.6	0.3	0.3	50.0
	13	2.7	4.0	2.7	3.0	1.3	0.3	1.0	76.9
	19	2.6	4.0	2.6	3.2	1.4	0.6	0.8	57.1
	25	2.5	4.0	2.5	3.1	1.5	0.6	0.9	60.0
	31	2.5	3.9	2.5	3.0	1.4	0.5	0.9	64.3
1800	1	2.9	2.9	2.9	2.9	0.0	0.0	0.0	0.0
	7	2.4	3.4	2.4	2.9	1.0	0.5	0.5	50.0
	13	2.4	3.8	2.4	3.0	1.4	0.6	0.8	57.1
	26	2.6	3.5	2.6	2.8	0.9	0.2	0.7	77.7
	32	3.5	4.2	3.5	3.7	0.7	0.2	0.5	71.4

* Only 2 animals in the entire series showed no evidence of growth retardation after a sufficient interval following irradiation. It is possible that these animals moved sufficiently during treatment so that the knee did not receive the expected dosage. They are excluded from Table III.

lated in percentage of the normal growth as determined in the untreated extremity) increased roughly in proportion to the dosage used (Fig. 11). There was some individual variation in this regard, however; a few animals showed a proportionately

TABLE II

MEASUREMENTS OF TIBIAE FOLLOWING IRRADIATION OF NINETY DAY OLD RATS

Dosage in Roentgens	Duration of Experiments in Weeks	Untreated Tibiae Length in cm.		Treated Tibiae Length in cm.		Length increment in cm.			Percentage Retardation c/a
		Before	After	Before	After	Untreated a	Treated b	Difference c	
665	5	3.3	3.7	3.3	3.7	0.4	0.4	0.0	0.0
	11	3.3	4.0	3.3	3.8	0.7	0.5	0.2	28.5
	17	3.1	4.0	3.1	3.8	0.9	0.7	0.2	22.2
	30	3.1	4.1	3.1	3.9	1.0	0.8	0.2	20.0
	36	3.1	4.1	3.1	3.8	1.0	0.7	0.3	30.0
835	2	3.1	3.5	3.1	3.5	0.4	0.4	0.0	0.0
	8	3.2	3.8	3.2	3.6	0.6	0.4	0.2	33.3
	14	3.3	4.0	3.3	3.9	0.7	0.6	0.1	14.3
	20	3.2	3.9	3.2	3.7	0.7	0.5	0.2	28.5
1000	5	3.1	3.6	3.1	3.4	0.5	0.3	0.2	40.0
	11	3.1	3.7	3.2	fract.	0.6			
	17	3.2	3.9	3.2	3.5	0.7	0.5	0.2	28.5
	23	3.2	3.8	3.2	3.6	0.6	0.4	0.2	33.3
	36	3.1	4.2	3.1	4.0	1.1	0.9	0.2	18.2
1165	1	3.6	3.7	3.6	3.7	0.1	0.1	0.0	0.0
	8	3.4	3.9	3.4	3.6	0.5	0.4	0.1	20.0
	14	3.4	3.9	3.4	3.5	0.5	0.1	0.4	80.0
	20	3.6	4.0	3.6	3.8	0.4	0.2	0.2	50.0
	26	3.4	4.1	3.4	3.8	0.7	0.4	0.3	42.9
	33	3.2	4.0	3.2	3.6	0.8	0.4	0.4	50.0
1335	5	3.1	3.6	3.1	3.4	0.5	0.3	0.2	40.0
	11	3.1	3.7	3.1	3.4	0.6	0.3	0.3	50.0
	17	3.4	4.1	3.4	3.8	0.7	0.4	0.3	42.9
	36	3.2	3.9	3.2	3.5	0.7	0.3	0.4	57.1
1500	2	3.1	3.5	3.1	3.4	0.4	0.3	0.1	25.0
	8	3.1	3.8	3.1	3.4	0.7	0.3	0.4	57.1
	14	3.2	3.9	3.2	3.5	0.7	0.3	0.4	57.1
	20	3.3	4.0	3.3	3.6	0.7	0.3	0.4	57.1
	26	3.3	3.7	3.3	3.7	0.4	0.4	0.0	0.0*
	32	3.7	4.3	3.7	3.8	0.6	0.1	0.5	83.3
1800	2	3.0	3.3	3.0	3.1	0.3	0.1	0.2	66.6
	8	3.3	3.8	3.3	3.6	0.5	0.3	0.2	40.0
	14	3.2	4.2	3.2	3.6	1.0	0.4	0.6	60.0
	21	3.2	4.1	3.2	3.9	0.9	0.7	0.2	22.2
	27	3.2	4.0	3.2	3.4	0.8	0.2	0.6	75.0
	33	3.3	4.2	3.3	3.7	0.9	0.4	0.5	55.5

* Only 2 animals in the entire series showed no evidence of growth retardation after a sufficient interval following irradiation. It is possible that these animals moved sufficiently during treatment so that the knee did not receive the expected dosage. They are excluded from Table III.

greater amount of retardation than others given similar dosage. The average percentage growth retardation in 56 animals sacrificed eight or more weeks after irradiation is given in Table III. This interval (eight weeks) was chosen since the major

Table III

AVERAGE PERCENTAGE RETARDATION OF TIBIAL GROWTH IN FIFTY-SIX ANIMALS SACRIFICED EIGHT OR MORE WEEKS AFTER IRRADIATION

Dosage in Roentgens	30 day old		90 day old		30 and 90 day groups	
	No.	Percentage Retardation	No.	Percentage Retardation	No.	Percentage Retardation
665	4	17.0	4	25.2	8	21.1
835	4	24.3	3	25.4	7	24.7
1000	6	33.9	3	26.7	9	31.2
1165	4	47.9	5	48.6	9	48.3
1335	2	35.1	3	50.0	5	44.0
1500	4	64.6	4	63.6	8	64.1
1800	3	68.7	5	50.5	8	57.4

portion of retarding effects of roentgen irradiation on growth was attained in all instances before this time. It will be noted from Tables I and II that the maximal percentage of retardation was about 60 to 80 per cent. The remaining 20 to 40 per cent of growth increment which occurred in all the treated extremities was undoubtedly due in large part to growth from the distal tibial epiphyseal plate which received no irradiation.

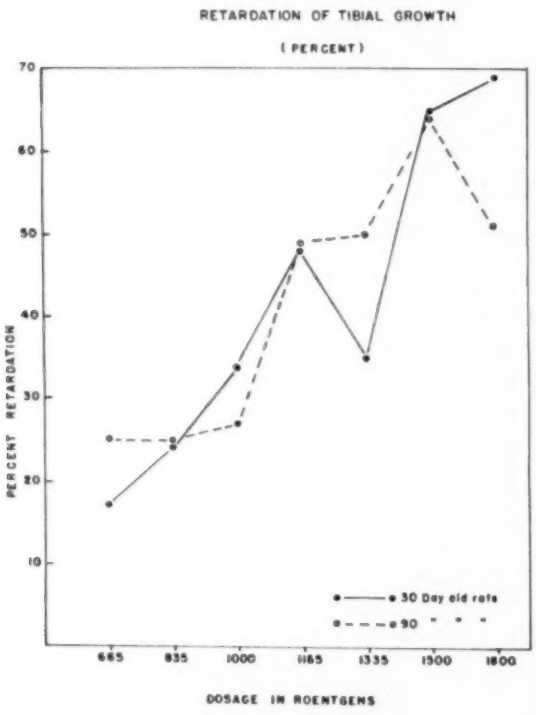

Fig. 11

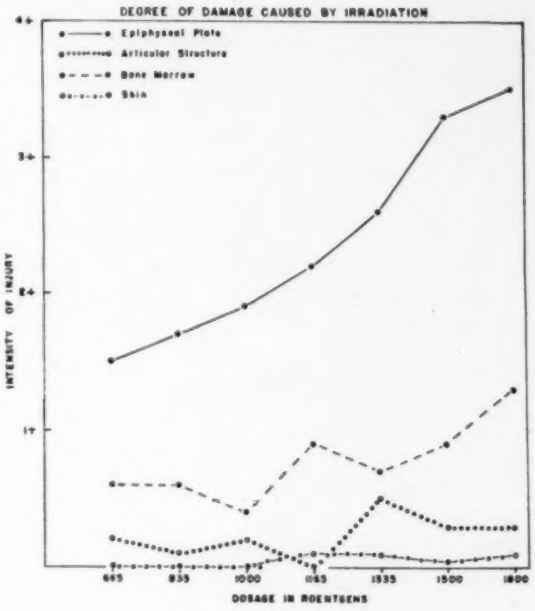

Fig. 12

The ultimate disparity in lengths of the treated and untreated tibiae, as one might expect, was most marked in those treated at thirty days of age. In the 180 day old animals growth was so slow that, although retardation was observed, its accurate measurement was not possible.

An unexpected finding was the similarity in the percentage retardation with equal doses in the two age groups measured. The younger, more actively growing epiphyseal plate in the thirty day old animal would be expected to suffer greater damage than the more mature and less rapidly growing epiphyseal plate of the ninety day old animal when exposed to the same amount of irradiation. This expectation, however, was not borne out by the results of this study. Although the ultimate difference in length of the treated and untreated extremities was greater in the thirty day old animals, when the retardation was plotted in percentage of normal growth the amount of retardation was found to be the same for both age groups (Fig. 1 and Table III). The amount of damage sustained by the growing

epiphyseal plate by irradiation was dependent on the dosage but not on the age of the animal. The fact is of considerable importance to radiologists in the treatment of various lesions in children when the field of irradiation includes a growing epiphyseal plate.

Sections of skin from both directly (medial) and indirectly (lateral) treated portions of the same extremity revealed no evidence of significant injury with the doses used. The epidermis remained intact, there was no permanent atrophy of skin appendages or sustentative elements, and late sequelae were not encountered. Hematopoietic activity within bone marrow in the field of treatment was not seriously impaired. Interference with the blood forming function in a small area of a long bone in a human subject would have no appreciable influence upon the physiologic capacity of the individual. Marrow and cortical vascular channels exhibited little or no variation from the normal. The effects produced in this series upon all of these structures may therefore be safely considered to have no major clinical significance.

The synovia of the knee joint and the joint relations in general were undisturbed. Although with the higher doses articular cartilage exhibited very minor focal areas of degeneration, these were likewise observed in many untreated limbs. They were, therefore, probably of slight significance. Certainly the frequency with which they appeared in those rats receiving 1,165 r or less was not greater than that observed normally.

It is of primary importance to determine conclusively whether or not delayed degenerative changes might be precipitated by either the direct effect of the irradiation upon joint structures or as the result of secondary change related to altered bone growth. These detrimental features have not appeared within a period of nine months after irradiation, an interval which may be considered to represent approximately one-fourth of the rat's normal life span. In order to insure against their production in human subjects similarly treated, however, additional experiments are at present in progress. In these, larger animals (dogs) are being employed and it is planned to observe them for a considerable period after epiphyseal fusion has become completed. It is necessary to state here that the first dog sacrificed recently has shown histologic evidence of injury to the cells of the articular cartilage although no grossly detectable damage appeared. It is our intention to refrain from applying our results clinically until these possibilities have been safely excluded.

SUMMARY AND CONCLUSIONS

A group of thirty, ninety and 180 day old albino rats were subjected to roentgen irradiation of one knee joint and the resultant changes studied histologically and roentgenographically. The epiphyseal plate is a very radiosensitive tissue. Doses of 665 to 1,165 r produced moderately severe histological changes while doses of 1,335 to 1,800 r caused very severe injury as evidenced by disruption of the cartilage cell columns and destruction of chondrocytes. There was no evidence indicating stimulation and only inconsequential evidence of regeneration of epiphyseal cartilage. Other tissues in the treated area—skin, subcutaneous tissue, muscle, synovia and articular cartilage—showed insignificant changes of a transitory nature (Fig. 2). The hematopoietic elements of the bone marrow in the treatment field were diminished but this local effect seemed to be of little significance to the organism as a whole. No degenerative or traumatic changes were noted in the treated joints even after nine months' observation.

Careful measurement of longitudinal growth of the tibia after irradiation showed that the doses used (665 to 1,800 r) all produced retardation of growth and that the retardation varied roughly proportionately to the irradiation administered. The larger doses 1,335 to 1,800 r seemed to produce essentially complete arrest of growth of the treated epiphysis.

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EDITORIAL

THE OBTURATOR SIGN IN THE EARLY ROENTGEN DIAGNOSIS OF SEPTIC ARTHRITIS OF THE HIP

THE importance of the psoas muscle shadow as a diagnostic aid in roentgenographic examinations in a suspected psoas abscess, a perinephric abscess, or retroperitoneal tumor is well known to all roentgenologists. However, the importance of soft tissue shadows in the pelvic area as seen in the anteroposterior projection in roentgenograms had been overlooked as an aid in the differential diagnosis until Hefke and Turner,[1] in a recent article, pointed out the importance of the soft tissue shadow just medial to the acetabulum on the inner aspect of the pelvis as an aid in the roentgen diagnosis of septic arthritis and in tuberculosis of the hip.

The border of this soft tissue shadow, as described by Hefke and Turner, ordinarily starts from a point lateral to and below the lower pole of the sacroiliac joint, follows the line of the pelvic inlet downward over the acetabulum, and disappears behind the upper ramus of the pubis. This shadow in normal children measures from 2 to 8 millimeters at its widest point, and usually the shadow on one side corresponds in width to the shadow on the other. There may, however, be a mir.imal difference in the width of these shadows in normal individuals.

In order to determine the exact structure which caused this shadow, Hefke and Turner made dissections on postmortem specimens and by the use of curved wires paced along the inner border of the psoas, and an anteroposterior roentgenogram, they were able to demonstrate that the psoas muscle did not correspond to the shadow described. Therefore the psoas was removed and another roentgenogram was obtained, and by a process of elimination they finally determined that the obturator internus muscle is definitely proved to be the substratum of the shadow.

These authors point out that it is well known that the tendon of the obturator passes immediately adjacent to the capsule of the hip and extension of the inflammatory process may well lead to a roentgenographically visible swelling of the obturator muscle.

The obturator sign, as described by Hefke and Turner, consists in a widening and a change in the contour of the normal obturator shadow. This widening may be very slight to very marked, and four gradations, from 1 to 4, were arbitrarily chosen as a basis for classification of their cases. Grade 2 was considered to include those cases in which the shadow was approximately twice the normal width; Grade 4, more than four times the normal, and Grades 1 and 3 were placed correspondingly. In the interpretation of changes in the obturator muscle the shadows of the uninvolved hip area were taken as normal.

In a small number of cases it was noted that the obturator shadow was obscured, and after an analysis of their cases they came to the conclusion that the obscured obturator shadow is a positive finding indicative of a pathological condition of the hip joint.

The technique for routine anteroposterior roentgenograms of the pelvis was followed in their studies. No special advantage had been shown by using soft tissue technique. They point out the fact, however, which is only too obvious, that the pelvis must be level or one obturator may be thrown into higher relief than the other

[1] Hefke, H. W., and Turner, V. C. The obturator sign as the earliest roentgenographic sign in the diagnosis of septic arthritis and tuberculosis of the hip. *J. Bone & Joint Surg.*, 1942, *24*, 857–869.

one, which could bring about some confusion in the interpretation of the soft tissue shadow. In a number of their cases they found it of advantage to obtain an anteroposterior view of the pelvis with the hips in marked abduction, flexion to 90 degrees, and marked external rotation—the so-called "frog position" frequently used in obtaining lateral views of the hips. This position brings into greater relief the obturator shadow but in an acute septic condition involving the hip such a position may be out of the question because of the intense pain from which the patient suffers.

The importance of a correct diagnosis in septic arthritis of the hip warrants the use of any method or methods of examination which will help one to arrive at an early diagnosis before the devastating effects of the infection are manifest. In their study of the obturator sign 23 cases of septic arthritis of the hip served as the clinical basis. They found that the obturator sign is of greatest value during the early weeks of hip disease. At the end of the first two weeks it was possible to make a roentgen diagnosis of hip disease in 94 per cent of the cases, whereas using bone and joint changes alone, the diagnosis could have been made in only 25 per cent. The obturator sign was first found positive on the third day, joint changes on the fifth and bone changes on the eighth. Therefore the obturator sign in the experience of these authors is the earliest roentgenographic sign observed in septic arthritis of the hip.

The obturator sign is of less importance in the diagnosis of tuberculosis of the hip as the onset of this condition is so much less sudden and dramatic than septic arthritis, and unfortunately the first roentgenographic examination made in suspected cases of tuberculosis of the hip are delayed for weeks and at times even months after the onset of the initial symptoms.

In an analysis of their group of cases of tuberculosis of the hip they found that the obturator shadow was most frequently obscured, rather than showing a distinct bulging with sharply demarcated border, as is usually observed in cases of septic arthritis of the hip, and it was obvious from their studies that the obturator sign is of no great value in making a diagnosis of early tuberculosis of the hip inasmuch as both the bone and joint changes usually appear earlier and with greater frequency.

In Perthes' disease, in both the early and late stages, they observed no change in the obturator shadow and in slipping of the capital femoral epiphysis there was observed no change in the obturator shadow, and likewise in fractures of the pelvis, ischium, ilium, and femur close to the hip joint no pathologic change was observed in the obturator outline. In osteomyelitis of the pelvis not involving the neighboring hip joint no obturator involvement was noted. Also in soft tissue infection about the thigh with marked inguinal lymphadenopathy they observed no abnormality in the obturator shadow.

It is evident from the studies which Hefke and Turner have carried out that the obturator shadow becomes of the greatest value in the early roentgenographic diagnosis of septic hip disease and it is of utmost importance that this diagnostic sign be not overlooked as it appears to be one of the earliest roentgenographic signs in the diagnosis of septic arthritis of the hip. It is hoped that other observers will pay particular attention to the obturator sign as an additional aid in the roentgenographic diagnosis of septic arthritis of the hip.

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

Items for this section solicited promptly after the events to which they refer.

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Secretary, Dr. H. Dabney Kerr, University Hospital, Iowa City, Iowa. Annual Meeting: 1943, to be announced.

American College of Radiology
Secretary, Mac F. Cahal, 540 N. Michigan Ave., Chicago, Ill. Annual meeting: 1943, to be announced.

Section on Radiology, American Medical Association
Secretary, Dr. J. T. Murphy, 421 Michigan St., Toledo, Ohio. Annual meeting: 1943, cancelled.

Arkansas Radiological Society
Secretary, Dr. J. S. Wilson, Mack Wilson Hospital, Monticello, Ark. Meets every three months and also at time and place of State Medical Association.

Radiological Society of North America
Secretary, Dr. D. S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y. Annual meeting: 1943, to be announced.

Radiological Section, Baltimore Medical Society
Secretary, Dr. Walter L. Kilby, Baltimore. Meets third Tuesday each month, September to May.

Section on Radiology, California Medical Association
Secretary, Dr. J. D. Coate, 434 Thirtieth St., Oakland, Calif.

Radiological Section, Connecticut Medical Society
Secretary, Dr. Max Climan, 242 Trumbull St., Hartford, Conn. Meets bi-monthly on second Thursday, at place selected by Secretary. Annual meeting in May.

Section on Radiology, Illinois State Medical Society
Secretary, Dr. H. W. Ackemann, 321 W. State St., Rockford, Ill.

Radiological Section, Los Angeles County Medical Association
Secretary, Dr. Donald R. Laing, 65 North Madison Ave., Pasadena, Calif. Meets on second Wednesday of each month at the County Society Building.

Radiological Section, Southern Medical Association
Secretary, Dr. Roy G. Giles, Temple, Texas.

Brooklyn Roentgen Ray Society
Secretary, Dr. Leo Harrington, 880 Ocean Ave., Brooklyn, N. Y. Meets monthly on fourth Tuesday, October to April.

Buffalo Radiological Society
Secretary, Dr. Joseph S. Gian-Francheschi, 610 Niagara St., Buffalo, N. Y. Meets second Monday of each month except during summer months.

Chicago Roentgen Society
Secretary, Dr. Warren W. Furey, 6844 S. Oglesby Ave., Chicago, Ill. Meets second Thursday of each month October to April inclusive at the Palmer House.

Cincinnati Radiological Society
Secretary, Dr. Samuel Brown, 707 Race St., Cincinnati, Ohio. Meets third Tuesday of each month, October to May, inclusive.

Cleveland Radiological Society
Secretary, Dr. J. O. Newton, 13921 Terrace Rd., East Cleveland. Meets at 6:30 P.M. at Midday Club on fourth Monday each month, October to April, inclusive.

Denver Radiological Club
Secretary, Dr. Edward J. Meister, 366 Metropolitan Bldg., Denver, Colo. Meets third Friday of each month at Denver Athletic Club.

Detroit Roentgen Ray and Radium Society
Secretary, Dr. E. R. Witwer, Harper Hospital. Meets monthly on first Thursday from October to May, at Wayne County Building.

Florida Radiological Society
Acting Secretary, Dr. Walter A. Weed, 204 Exchange Bldg., Orlando, Fla. Meetings in May and November.

Georgia Radiological Society
Secretary, Dr. R. C. Pendergrass, Prather Clinic Bldg., Americus, Ga. Meets in November and at annual meeting of Medical Association of Georgia in the spring.

Radiological Society of Kansas City
Secretary, Dr. Arthur B. Smith, 800 Argyle Bldg., Kansas City, Mo. Meets third Thursday of each month at a place designated by the president.

Illinois Radiological Society
Secretary, Dr. Wm. DeHollander, St. John's Hospital, Springfield, Ill. Meets three times a year.

Indiana Roentgen Society
Secretary, Dr. H. C. Ochsner, Methodist Hospital, Indianapolis. Meeting held the second Sunday in May annually.

Kentucky Radiological Society
Secretary, Dr. W. C. Martin, 321 W. Broadway, Louisville. Meets annually in Louisville on first Saturday in April.

Long Island Radiological Society
Secretary, Dr. Marcus Wiener, 1430-48th St., Brooklyn, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:30 P.M.

Louisiana Radiological Society
Secretary, Dr. J. R. Anderson, 1130 Louisiana Ave., Shreveport. Meets annually during Louisiana State Medical Society Meeting.

Michigan Association of Roentgenologists
Secretary, Dr. E. M. Shebesta, 1429 David Whitney Bldg., Detroit. Three meetings a year, Fall, Winter, Spring.

Milwaukee Roentgen Ray Society
Secretary, Dr. C. A. H. Fortier, 231 W. Wisconsin Ave., Milwaukee, Wis. Meets monthly on second Monday at University Club.

Minnesota Radiological Society
Secretary, Dr. J. P. Medelman, 572 Lowry Medical Arts Bldg., St. Paul.

Nebraska Radiological Society
Secretary, Dr. D. A. Dowell, Medical Arts Bldg., Omaha, Nebr. Meets third Wednesday of each month, at 6 P.M. at either Omaha or Lincoln.

New England Roentgen Ray Society
Secretary, Dr. Hugh F. Hare, Lahey Clinic, Boston, Mass. Meets monthly on third Friday, Boston Medical Library.

Radiological Society of New Jersey
Secretary, Dr. H. J. Perlberg, 921 Bergen Ave., Jersey City. Meets annually at time and place of State Medical Society. Mid-year meetings at place chosen by president.

New York Roentgen Society
Secretary, Dr. M. M. Pomeranz, 1020 Park Ave., New York City. Meets monthly on third Monday, New York Academy of Medicine, at 8:00 P.M.

North Carolina Roentgen Ray Society
Secretary, Dr. Major Fleming, Rocky Mount, N. C. Annual meeting at time and place of State Medical Society. Mid-year scientific meeting at place designated.

North Dakota Radiological Society
Secretary, Dr. L. A. Nash, St. John's Hospital, Fargo. Meetings held by announcement.

Central New York Roentgen Ray Society
Secretary, Dr. C. F. Potter, 820 S. Crouse Ave., Syracuse. Three meetings a year. January, May, November.

* Secretaries of Societies not here listed are requested to send the necessary information to the Editor.

Ohio Radiological Society
Secretary, Dr. J. E. McCarthy, 707 Race St., Cincinnati. Meets at time and place of annual meeting of Ohio State Medical Association.

Pacific Roentgen Society
Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

Pennsylvania Radiological Society
Secretary, Dr. L. E. Wurster, 416 Pine St., Williamsport.

Philadelphia Roentgen Ray Society
Secretary, Dr. R. P. Barden, University Hospital. Meetings first Thursday of each month from October to May inclusive at 8:15 P.M., in Thompson Hall, College of Physicians, 19 S. 22d St.

Pittsburgh Roentgen Society
Secretary, Dr. R. G. Alley, 4800 Friendship Ave. Meets second Wednesday each month, 4:30 P.M., October to June, Pittsburgh Academy of Medicine.

Rochester Roentgen Ray Society, Rochester, N. Y.
Secretary, Dr. Sidney Larson, Strong Memorial Hospital. Meets monthly on third Monday from October to May, inclusive, 8 P.M. at Strong Memorial Hospital.

Rocky Mountain Radiological Society
Secretary, Dr. A. M. Popma, 220 N. First St., Boise, Idaho.

St. Louis Society of Radiologists
Secretary, Dr. W. K. Mueller, University Club Bldg. Meets fourth Wednesday of each month, except June, July, August, and September, at a place designated by the president.

San Francisco Radiological Society
Secretary, Dr. H. A. Hill, 450 Sutter St., San Francisco. Meets monthly on third Thursday at 7:45 P.M., first six months at Toland Hall, second at Lane Hall.

South Carolina X-Ray Society
Secretary, Dr. T. A. Pitts, Baptist Hospital, Columbia, S. C. Meets in Charleston on first Thursday in November, also at the time and place of South Carolina State Medical Association.

Tennessee Radiological Society
Secretary, Dr. J. M. Frère, 707 Walnut St., Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

Texas Radiological Society
Secretary, Dr. L. W. Baird, Scott and White Clinic. Temple, Texas.

University of Michigan Department of Roentgenology Staff Meeting
Meets each Monday evening from September to June, at 7 P.M. at University Hospital.

University of Wisconsin Radiological Conference
Secretary, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets every Thursday from 4:00–5:00 P.M., Room 301, Service Memorial Institute.

Virginia Radiological Society
Secretary, Dr. C. H. Peterson, 603 Medical Arts Bldg., Roanoke, Va. Meets annually in October.

Washington State Radiological Society
Secretary, Dr. K. J. Holtz, American Bank Bldg., Seattle. Meets fourth Monday each month, College Club, Seattle.

X-ray Study Club of San Francisco
Secretary, Dr. J. M. Robinson, University of California Hospital. Meets monthly in evening on third Thursday.

Cuba

Sociedad de Radiología y Fisioterapia de Cuba
President, Dr. J. Manuel Viamonte, Hospital Mercedes, Habana, Cuba. Meets monthly in Habana.

British Empire

British Institute of Radiology Incorporated with the Röntgen Society
Meets monthly on third Thursday from November to June inclusive, at 8:15 P.M., 32 Welbeck St., London.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets on the third Friday of each month during the winter at 8:15 P.M. at the Royal Society of Medicine 1, Wimpole St., London, W. 1.

Faculty of Radiologists
Secretary, Dr. M. H. Jupe, 32 Welbeck St., London, W. 1 England.

Section of Radiology and Medical Electricity, Australasian Medical Congress
Secretary, Dr. H. M. Cutler, 139 Macquarie St., Sydney, New South Wales.

Radiological Section of the Victorian Branch of the British Medical Association
Secretary, Dr. Keith Hallam, St. George's Hospital, K.E.W., Melbourne, E. 4, Victoria, Australia. Meets monthly from March to November inclusive.

Canadian Association of Radiologists
Secretary, Dr. A. D. Irvine, 540 Tegler Bldg., Edmonton Alberta.

Section of Radiology, Canadian Medical Association
Secretary, Dr. C. M. Jones, Inglis St., Ext. Halifax, N. S.

Radiological Section, New Zealand British Medical Association
Secretary, Dr. Colin Anderson, Invercargill, New Zealand. Meets annually.

Continental Europe

Sociedad Espanola de Radiologia y Electrologia
Secretary, Dr. J. Martin-Crespo, Fuencarral, 7. Madrid, Spain. Meets monthly in Madrid.

Société Suisse de Radiologie (Schweizerische Röntgen-Gesellschaft)
Secretary for French language, Dr. A. Grosjean La Chaux de Fonds.
Secreatry for German language, Dr. Scheurer, Molzgasse Biel. Meets annually in different cities.

Societatea Romana de Radiologie si Electrologie
Secretary, Dr. Oscar Meller, Str. Banul Mărăcine, 30, S. I., Bucuresti, Roumania. Meets second Monday in every month with the exception of July and August.

All-Russian Roentgen Ray Association, Leningrad, USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson. Meets annually.

Leningrad Roentgen Ray Society
Secretaries, Drs. S. G. Simonson and G. A. Gusterin. Meets monthly, first Monday at 8 o'clock, State Institute of Roentgenology and Radiology, Leningrad.

Moscow Roentgen Ray Society
Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky. Meets monthly, first Monday, 8 P.M.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association.

BULLETIN OF THE AMERICAN COLLEGE OF RADIOLOGY

AN OPEN LETTER TO RADIOLOGISTS

The cornerstone of modern medical care is correct diagnosis, and the keystone of correct diagnosis is competent radiology. Competent radiology requires that there be adequate numbers of trained radiologists available both for patients outside hospitals and patients inside hospitals. As far as outside patients are concerned, there are fortunately hundreds of well trained conscientious radiologists in private practice who are doing good work and, as far as can now be told, will continue to do good independent American medical work in the future.

When we turn to the hospital situation the picture is somewhat different. There are hundreds of competent radiologists in American hospitals today, but many of them are *not* conducting their own practices. They have not the right to decide who shall be appointed as technicians and nurses in their departments, they cannot always decide the kind of equipment with which they must operate, and they often cannot decide the extent of the services which they believe they should render to patients, or the fees they should charge for those services. In other words, the departments of radiology are no longer under the direction of the radiologist in many hospitals—they are under the direction of the hospital superintendent.

If this were just a matter of fees or financial reward it might, with the altruistic traditions of the medical profession, well be overlooked. However, it obviously goes beyond that. He who pays the piper calls the tune. Precedents created today, especially in connection with group hospitalization insurance, may be frozen into our medical picture tomorrow.

What then should we do? The first and foremost obligation on every hospital radiologist is to do good medical work and to see that in every manner possible he keeps radiology identified as a medical specialty, as a branch of medicine and not as a branch of hospital work. He should pay as much attention to the organization side of his department as he does to the scientific side. If he is indifferent, or too busy, or too lazy to attend to the organization side he will find that in the eyes of the average layman, the average hospital superintendent, yes and even in the eyes of doctors, he is not in charge of his own department. More and more laymen and physicians are coming to regard radiology as a part of hospital service and not medical care. This is largely our own fault. (We are referring not to one or two large research or diagnostic clinics, but the average private hospital throughout the land.)

Again we ask, what should be done about it? We would suggest that for the sake of the scientific future of radiology in hospitals, as well as for the sake of the rights of the rest of our profession we should not consent to the inclusion of our services in any formally organized hospital insurance scheme. This will require courageous action and constant vigilance. The radiologist cannot always control details of practice as far as ordinary hospital in-patients are concerned. However, when a Blue Cross plan or a health insurance scheme gets started, the radiologist should go to his local county medical society and ask it not to approve any scheme that attempts to provide medical services (whether they be surgery or roentgen ray) as a part of hospitalization benefits. And, if they are already included, seek their exclusion or segregation. The crux of the Blue Cross plan problem is that many Blue Cross plans provide not group hospitalization, but hospitalization plus diagnostic-medical-care and in so providing will inevitably and ultimately control hospital radiology.

Think of it: ten million Americans are now covered by Blue Cross plans. In another decade twenty-five million Americans will be so covered. Instead of having diagnostic radiology benefits as an in-patient, they will be extended to out-patients also. Why? To avoid abuse of hospital beds.

Today, many subscribers *are* being hospitalized *only* because they are entitled to free roentgen-ray services. By offering outpatient roentgen-ray services, the hospital will be able to reduce bed occupancy.

To further reduce hospital costs, more and more radiologists will be hired and fired on the basis of the cheapest salary they will accept and not on their professional qualifications. The caliber of diagnostic medicine will suffer as the caliber of radiology declines.

Therefore, for purely scientific considerations alone, for the welfare of the specialty you have chosen, please awake to the vital necessity of having your service identified as a medical service, especially in Blue Cross plans. The present economic arrangements in medical practice have never come up for formal approval by a county or state medical society. But Blue Cross plans have. Observe that the American Medical Association has never approved a single Blue Cross plan. Why? Because the American Medical Association knows that if the Blue Cross plans can sell radiology today, and secure approval, they can sell surgery and ordinary medical care tomorrow, and demand approval. In no time they could control the entire practice of medicine. A group of laymen or corporations (always "not-for-profit") could dictate how and where medical practice should be conducted in this country.

Let us give group hospitalization our ardent support—when it *is* group hospitalization. There are today many communities, notably Kansas, Missouri, Washington, D. C., Michigan, Florida and California, where radiology is either not sold at all in connection with group hospitalization, or if sold is provided as a medical benefit along with, but not as a part of, hospital service. Checks for medical services are payable to medical men. Therefore, the group hospitalization corporation makes checks for radiology in hospitals payable to medical men. If he is on a salary or percentage basis he merely endorses the check and turns it over to the hospital treasury. If he is on a lease or rental basis he deposits the check to his account as would any other professional man. The importance of the distinction is exquisite. You are urged to ponder this problem and to take action now. You will be appalled to hear that some radiologists in one of our midwestern states have actually requested the local group hospitalization concern to make the checks payable to the hospital and not themselves. What incredible myopia!

Radiologists please awake. Our number one problem is to win the war. Our number two problem is to prevent the destruction of scientific practice and of diagnostic medical care for generations to come. No layman, no Blue Cross director can be expected to understand that radiology is the practice of medicine, and that you as radiologists have any professional rights whatsoever! You have to tell them these things and tell them repeatedly. Just as all freedom loving people have to fight for their freedom at regular intervals, almost every generation, so we, as members of the youngest and most rapidly developing specialty in medicine, have to fight for our own rights, and can proudly do so knowing that we are fighting for the rest of medicine at the same time.

Remember, ignoring entirely your own personal tastes in the matter and your own disregard for income, you should still awaken to the fact that the scientific side of your practice requires that it remain identified as a medical practice and not become a hospital one. To so identify it, you should collect your own fees and request all insurance companies, Blue Cross plans, hospitalization companies, and so forth, to make checks for medical services payable to medical men, that is, checks for radiological services payable to radiologists. And by payment is meant the entire sum and not any artificial division of medicine or surgery into technical and professional. The surgeon performs many technical procedures in his work and yet it would be absurd and destructive of his practice if

it were attempted to divide it into technical and professional. The same applies to radiology. In the words of the American College of Surgeons, each doctor concerned in the care of a patient should give or send directly to the patient a detailed statement showing the charges for services rendered. Your colleagues in private practice do so today. Will you in your hospital practice not seek to do likewise?

L. Henry Garland, M.D., Chairman
Commission on Hospital Standards,
American College of Radiology

STRAY RADIATION IN FLUOROSCOPIC ROOM

As an advisory member for the Committee on Safety and Standards, I wish to make the following supplementary report:

Recent studies of fluoroscopic roentgen-ray units have demonstrated the advisability of calling attention to stray radiation received per week by each occupant of the fluoroscopic room.

It has been found that when the shutters are opened to the limit, in order to cover the fluoroscopic screen near the table top, they will allow radiation to pass beyond the screen when moved away from the table top unless there is an automatic arrangement attached to the movement of the screen to control the opening of the shutters. If the roentgenologist is careful to keep the shutters closed so that the field of radiation is still visible, at all times, there will be no radiation passing beyond the screen. Roentgenologists often have a habit of opening the shutters wide when taking the first look, regardless of the position of the screen.

Considerable stray radiation may be scattered from the diaphragm opening and the patient. If the diaphragm opening is not well protected with lead to the table top, radiation will be scattered to those standing near the table. Lead aprons will absorb this radiation. Tests may be made by all the occupants of the fluoroscopic room by wearing dental films for a week. If the dental films are sufficiently blackened so that it is impossible to read ordinary print through the film, they have probably received more than 0.4 to 0.5 r.

J. L. Weatherwax, *Physicist*

AMERICAN COLLEGE OF PHYSICIANS

The Board of Regents of the American College of Physicians has announced the cancellation of their 1943 Annual Session, which was scheduled to be held in Philadelphia, April 13–16, 1943. This action was taken after thoughtful consideration of all factors involved, including an intimation from the Secretary of War and the Office of Transportation that larger national medical groups should not plan meetings at the time set; a growing difficulty in getting speakers and clinicians of top rank to maintain the usual standards of the program; prospect of greatly reduced attendance, because civilian doctors are faced with too great a burden of teaching and practice already; a decreasing active membership, due to approximately 25 per cent of all doctors being called to active military service. President James E. Paullin announced, however, that all other activities of the College would be pursued with even greater zeal, and that the College would especially promote regional meetings over the country and organize postgraduate seminars in the various military hospitals for doctors in the Armed Forces.

UROLOGY AWARD

The American Urological Association offers an annual award "not to exceed $500" for an essay (or essays) on the result of some specific clinical or laboratory research in Urology. The amount of the prize is based on the merits of the work presented, and if the Committee on Scientific Research deem none of the offerings worthy, no award will be made. Competitors shall be limited to residents in urology in recognized hospitals and to urologists who have been in such specific practice for not more than five years.

Essays must be in the hands of the Secretary, Dr. Thomas D. Moore, 899 Madison Avenue, Memphis, Tennessee, on or before March 1, 1943.

Miley B. Wesson
Chairman, Committee on Scientific Research

AMERICAN BOARD OF RADIOLOGY

The Board of Trustees of the American Board of Radiology has decided to continue examinations during the emergency, and will therefore conduct an examination during April, May or June of 1943. An attempt will be made to hold the examination at a place most convenient to the majority of the candidates.

Those wishing to be examined at the spring examination must have their application on file by March 1, 1943. Address all communications to Dr. B. R. Kirklin, Secretary, American Board of Radiology, Mayo Clinic, Rochester, Minnesota.

BOOK REVIEWS

Books sent for review are acknowledged under: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interest of our readers as space permits.

AN X-RAY ATLAS OF SILICOSIS. By Arthur J. Amor, M.D., (Lond.), M. Sc. (Wales), Honorary Physician, Clydach Memorial Hospital; Medical Officer, Mond Nickel Company, Ltd., Swansea. With translation of the Legends into French by Robert E. Horne, M. A. (Wales), Medical Secretary, Mond Nickel Company, Ltd., Swansea. With a foreword by Sir Wilson Jameson, M.A., M.D. (Aberdeen), F.R.C.P., of the Middle Temple, Barrister-at-Law; Dean of the London School of Hygiene and Tropical Medicine. Cloth. Price, $8.00. Pp. 206, with 72 illustrations. Baltimore: Williams & Wilkins Company, 1941.

This Atlas of Silicosis was written to describe the essential roentgenologic features of silicosis for senior medical students, industrial physicians, and those dealing with this type of disease.

The author has described briefly the etiology, pathology, roentgen manifestations, and clinical findings in silicosis and some of the nonspecific pneumoconioses. No effort has been made to go into detail concerning many of the aspects of this subject. He has, however, given sufficient information in the first four chapters to stimulate one to look elsewhere, if one is interested in this subject. The average physician is not familiar with the roentgen findings in a number of these conditions. Therefore, the author has devoted the major portion of his book to illustrating representative chest films and has given the history of these cases in both English and French.

The publishers have selected a very good print for this book, but the paper is very glossy and it is exceedingly difficult to read unless the light is just right. In selecting a calendar of paper for the illustrations the publishers have done an excellent job. Anyone familiar with reproducing the roentgen findings in silicosis is aware of the difficulties. In spite of this the author has been successful in most instances.

EUGENE P. PENDERGRASS

MALIGNANT DISEASE AND ITS TREATMENT BY RADIUM. By Stanford Cade, F.R.C.S., Surgeon, Westminster Hospital, Mount Vernon Hospital, and The Radium Institute; Lecturer in Surgery, Westminster Hospital Medical School; Associate Examiner in Surgery, University of London, etc. Cloth. Price, $18.00. Pp. 1280, with 623 illustrations, many in colour. Baltimore: Williams & Wilkins Company, 1940.

This ambitious volume includes information gained from the treatment of 3,000 cases of malignant disease cared for at Westminster Hospital, Mount Vernon Hospital and elsewhere in England. These patients all received radiation therapy alone or a combination of irradiation and surgery. The first 94 pages deal with the radioactivity of radium and include chapters on mass units, dosimetry and the measurements of plaques by Dr. H. T. Flint, Dr. C. W. Wilson and Dr. L. H. Gray. All doses are expressed in roentgens but unfortunately the difference between x-ray roentgens and gama-ray roentgens is not emphasized. Although a sketchy description of practical dosage calculation is given, the student will find it practically impossible to estimate actual tissue doses from the data provided.

The second section, comprising 180 pages, is entitled "The Biological Effects of Radiation" and deals with radiosensitivity, the mode of action of radiation, the effects of radium on normal and malignant tissues and radiation protection. The effects of over-irradiation of certain portions of the body are described in great detail, but this portion of the volume is incomplete. For instance, no mention is made of over-irradiation of the intestine, which constitutes one of the most important sequelae observed in actual practice.

The remainder of the book is divided into 20 chapters devoted to the clinical picture, pathology and treatment of malignant disease as it appears in the various anatomical locations. The material is well presented and techniques are illustrated so that they can be easily dupli-

cated, but the method of dosage calculation in terms of gamma-ray roentgens is still not clarified. The outstanding contribution of the volume consists of a convincing demonstration of the efficiency of multiple weak, heavily filtered radium needles and capsules used for relatively long periods of time. In no other publication can one find such a wealth of information relative to the indications for the use of this method in the treatment of cancer. This good feature is somewhat marred by the author's preference of the radium bomb for external irradiation, a preference which does not seem to be upheld by his recorded results.

The book is printed on a good grade of paper and the illustrations, many of which are in color, are unusually well done. The pathology and clinical classifications of the various types of cancer are adequately covered and although little American literature is included, an extensive bibliography is given at the end of each chapter. If the alleged superiority of teleradium be discounted this text will be found especially valuable by the radiologist who must work with relatively small amounts of radium.

Charles L. Martin

The 1941 Year Book of Radiology. *Diagnosis*, Edited by Charles A. Waters, M.D., Associate in Roentgenology, Johns Hopkins University; Assistant Visiting Roentgenologist, Johns Hopkins Hospital; Associate Editor, Whitmer B. Firor, M.D., Assistant in Roentgenology, Johns Hopkins University; Assistant in Roentgenology, Johns Hopkins Hospital. *Therapeutics*, Edited by Ira I. Kaplan, B.Sc., M.D., Director, Radiation Therapy Department, Bellevue Hospital, New York City; Associate Radiologist, Lenox Hill Hospital, New York City; Clinical Professor of Surgery, New York University Medical College. Cloth. Price, $5.00. Pp. 440, with 486 illustrations. Chicago: Year Book Publishers, Inc., 1941.

The 1941 Year Book of Radiology has been in use for several months and most radiologists are aware of its contents. In view of its widely recognized usefulness it needs hardly more than a routine announcement. Those about to enter on the specialty should know that in this one book is contained more information in condensed form than could be obtained from any other single source or indeed from many more sources than are available to the average physician. In fact 80 scientific publications have been searched by the capable staffs of Drs. Waters and Kaplan with the usual remarkable collection of interesting cases and aids to diagnosis and treatment.

The diagnostic section dealing with the osseous system alone contains so many interesting subjects that it is difficult to select those most interesting. So-called creeping fractures, pseudofractures, infarction of bones, hemangiomas, eosinophilic granulomas of bone, dorsal bunion, anomalies of occiput, axis and atlas are a few of the highlights of the osseous section.

The glandular, respiratory, gastrointestinal, genitourinary and other special divisions of the diagnostic portion contain fully as interesting an array of subjects. The chapter on military roentgenology needs no comment as to its timeliness.

Therapeutics surpasses if possible the high standards of previous years. Treatment of angina pectoris and hypertension, prevention of hearing defects by pharyngeal irradiation, roentgen therapy of glaucoma avoiding enucleation, treatment of bursitis and rheumatic disease, accurate forecasting of irradiation sickness are among the non-malignant conditions contained in Dr. Kaplan's section, and study and treatment of malignant conditions occupies its usual important share of space. As in former years the editorial comments following many of the abstracts aid the younger man in evaluating the facts and conclusions of the original authors and are an invaluable part of the work.

E. Walter Hall

Epilepsy and Cerebral Localization: A Study of the Mechanism, Treatment and Prevention of Epileptic Seizures. By Wilder Penfield, Litt. B., M.D. (Johns Hopkins), D. Sc. (Oxon., Princeton), Professor of Neurology and Neurosurgery, McGill University; Director of the Montreal Neurological Institute, and Theodore C. Erickson, M.A., M.Sc., M.D. (Minnesota), Ph.D. (McGill), Formerly Lecturer in Neurosurgery, McGill University; Assistant Surgeon, Montreal Neurological Institute; Now Associate Professor of Surgery, University of Wisconsin. Chapter xiv by Herbert H. Jasper; Chapter xx by M. R. Harrower-Erickson. Cloth. Price, $8.00. Pp. 623, with 163 illustrations. Springfield, Illinois: Charles C Thomas, 1941.

This scholarly volume should perhaps be entitled "Cerebral Localization and Epilepsy." The portion of the book which entitles it to a permanent place in medical literature is the series of excellent case reports illustrating the principles of cortical localization. No such group of well-recorded observations on the results of stimulation and extirpation of various portions of the brain has ever been reported.

The arrangement of the book tends to give the impression that the majority of cases of epilepsy are due to focal lesions susceptible of surgical removal. This impression is strengthened by the inclusion of an account of the relief of seizures by removal of brain tumors. The authors' experience with the control of seizures by surgical means has been unusually favorable —about 40 per cent in carefully selected cases. The authors remark: "Operations for the surgical removal of epileptogenic lesions of the brain, however incompletely developed, already offer a more encouraging and gratifying prospect to the neurosurgeon than does the radical treatment of brain tumors."

Relatively little attention is paid to the subject of cryptogenic or "idiopathic" epilepsy, which enormously outnumbers all other types. From the table on page 22, one would judge that cryptogenic seizures were to be suspected strongly only in the second decade. The proportion of spontaneous improvement is given at 2 per cent; this is lower than the figure given, for example, by Lennox, of 20 per cent. No comparison is given between the results of medical and those of surgical treatment. The authors are wholly skeptical of the value of medical treatment of seizures due to focal lesions, but in other clinics the results of such treatment are excellent.

There are extremely good special chapters on cranial roentgenography, electroencephalography, and of the results of psychological studies.

This book should be in the library of every neurologist, indeed of every physician interested in the important subject of seizures.

Tracy J. Putnam

DEPARTMENT OF TECHNIQUE

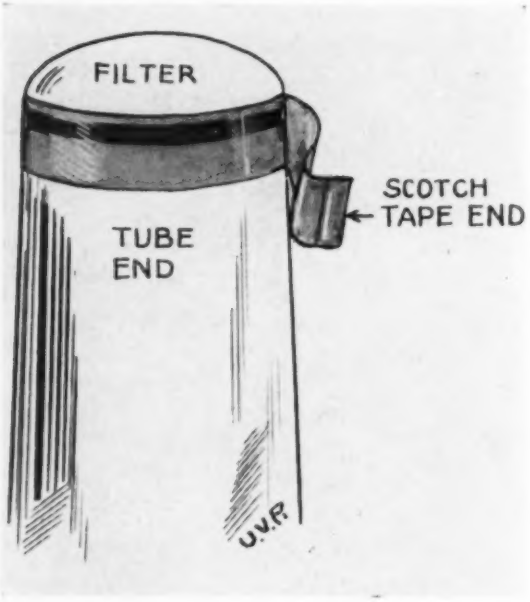
Department Editor: ROBERT B. TAFT, M.D., B.S., M.A., 103 Rutledge Ave.
Charleston, S. C.

A SIMPLE WAY TO HOLD A FILTER IN PLACE ON CONTACT THERAPY TUBES

By U. V. PORTMANN, M.D.
Cleveland Clinic
CLEVELAND, OHIO

WE HAVE been accustomed to hold a filter in place on the contact therapy tubes (Philips-Metalix) by slipping a finger cot over it and the tube end or to drop the filter into a localizing cone.

There are disadvantages to these methods. The thin rubber cot tears easily. It is becoming difficult to obtain cots of proper size. The filter sometimes gets out of alignment because it is not held securely enough. When an unattached filter is dropped into a localizing cone it may be inverted, which is annoying, and if not discovered will result in decreased dosage from increased distance.



These difficulties may be obviated by adjusting the concavo-convex filter on the tube end and wrapping a single short strip of half or quarter inch scotch cellulose tape around the rim of the filter and tube end as illustrated. This can be done quickly, the filter is held securely, it is clean and cheap. If a sterilized tube end is desirable, the filter may be attached as described, then a cot will slip over it easily. Protected in this way the rubber covered tube end may be immersed in a germicidal solution. It is easier to remove the tape if made longer than the circumference of the tube, then turned back on itself with adhesive surfaces in apposition thus making a small tab to grasp. Adhesive material sticking to the tube may be wiped away with alcohol or benzine.

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ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

ROENTGEN DIAGNOSIS

ABDOMEN

McNEILL, JAMES H. Persimmon phytobezoar with case report. *Ann. Int. Med.*, May, 1941, *14*, 2142–2147.

Persimmon phytobezoar is generally seen in the United States and in Japan where the persimmon is native. It is caused by eating whole persimmons when the stomach is empty. There is a soluble astringent called shibuol just beneath the skin of the persimmon which is coagulated by the action of the stomach acids and produces the phytobezoar. These bezoars are apt to cause peptic ulcer in the prepyloric region. The bezoar itself only causes vague stomach symptoms.

The author describes a case of his own and analyzes the symptoms from this case and 11 others reported in the literature. His patient, a man of fifty-seven, came for treatment in the spring for pain in the stomach, which he had had since the preceding fall. His symptoms suggested peptic ulcer. Roentgen examination showed a filling defect in the prepyloric region and a movable translucent mass in the stomach which was diagnosed as a pedunculated epithelioma, but which proved on operation to be a phytobezoar. The ulcer was resected, though these ulcers usually heal spontaneously after the removal of the bezoar. The patient reported that he had eaten a considerable amount of persimmons one day the preceding fall just before the beginning of the symptoms and had taken no food or drink for several hours afterward.—*Audrey G. Morgan.*

SCHINDLER, RUDOLF, STEINER, PAUL E., SMITH, WILLIAM M., and DAILEY, MORRIS E. The classification of gastric carcinoma. *Surg., Gynec. & Obst.*, July, 1941, *73*, 30–39.

The histological grading of carcinomata of the stomach in use up to this time has apparently failed to show the degree of clinical malignancy. Prognosis does not seem to depend on the size of the tumor, its site or its microscopic structure.

The authors suggest a classification based on macroscopic criteria. According to this classification Type I is polypoid carcinoma, characterized by a broad base, supporting a hard hemispherical swelling. This is found in 2.9 per cent of cases. Type II is the non-infiltrating carcinomatous ulcer which constitutes 17.6 per cent of all cases, Type III is infiltrating carcinomatous ulcer, which occurs in 16.3 per cent of all cases and Type IV is of the diffuse infiltrating type which constitutes 63.2 per cent of all cases.

A table is given showing a comparison between the macroscopic and microscopic grades in 50 cases. Apparently the end-results after surgery are very good in macroscopic Types I and II and not good in Types III and IV. Further study is necessary to confirm this impression, however, and more work should be done in correlating macroscopic types, microscopic grades and surgical results in an effort to establish a surgical prognosis before operation.—*Audrey G. Morgan.*

BRUNN, HAROLD, and GOLD, RUBIN L. The surgical problem of chronic gastritis. *Surg., Gynec. & Obst.*, Jan., 1941, *72*, 31–37.

Early diagnosis of cancer of the stomach is highly desirable. Gastroscopy is a valuable aid in differential diagnosis. But there are cases in which differentiation between gastritis and cancer is extremely difficult, not only on roentgen and gastroscopic examination but even on surgical exploration. Antral gastritis, a form of chronic hyperplastic gastritis, is probably precancerous.

One of the authors, in collaboration with Pearl, described the first case of hypertrophic gastritis simulating tumor fourteen years ago. Now after fourteen years the patient still has intermittent attacks of mild abdominal distress and diarrhea, which are controlled fairly well by bland diet and dilute hydrochloric acid. Three further cases are described, in 2 of which a diagnosis of cancer was made on the basis of the clinical and roentgen findings but in which operation showed severe hypertrophic gastritis. In the third case the first roentgen examination suggested a single gastric polyp. Gastroscopy showed evidence of diffuse infiltrative changes which, however, were interpreted as being

caused by gastritis. Four months later the roentgenogram showed pronounced changes and operation revealed an advanced inoperable carcinoma of the posterior wall of the stomach.

The fact that there are such difficult cases does not argue against the value of gastroscopy as an aid in diagnosis. If neither roentgen examination or gastroscopy makes definite diagnosis possible, exploratory operation is justified, not only for the purpose of settling the diagnosis but for that of removing a possible cancer.—*Audrey G. Morgan.*

Mullen, Thomas F. Some factors influencing the curability of cancer of the stomach. *Surg., Gynec. & Obst.*, Feb. 14, 1941, *72*, 298–306.

From 1920 to 1938 there has been a steady increase in the number of deaths from cancer. About one-third of these are from cancer of the stomach; there are more than 100 deaths from cancer of the stomach every day of the year.

It is probable that cancer never occurs in the normal stomach, but is preceded by various types of chronic gastritis. There are substances occurring normally in the body which, under the influence of disturbed metabolism, may become carcinogenic.

One of the necessary factors in the early detection and consequent curability of cancer of the stomach is a high index of suspicion on the part of both patient and physician. Many persons have so-called dyspepsia without thinking much about it. But the public should be taught that signs of gastric distress, loss of weight and appetite, vomiting, weakness and diarrhea are symptoms that require medical attention. Another group of patients do not have digestive symptoms, but only extreme fatigue and pernicious anemia.

And physicians themselves should recognize the fact that a roentgen study of the whole gastrointestinal tract is a necessary part of a complete physical examination, particularly if there are any digestive symptoms. Also that one negative result does not rule out cancer of the stomach. The examination should be repeated at regular intervals, preferably by the same expert roentgenologist, as long as there are symptoms. Finally, if cancer of the stomach is diagnosed it should be treated only by a surgeon of the greatest skill and experience. The average operative mortality is about 25 per cent. In skilled hands the operative mortality should be less than 15 per cent. Even if surgery is only a crude method, as long as no better method is known it should be carried out with the highest degree of skill and only by surgeons with experience in this particular field.—*Audrey G. Morgan.*

Bieren, Roland E. Carcinoma of the lower intestinal tract. *Surg., Gynec. & Obst.*, March, 1941, *72*, 611–615.

From January, 1922, to June, 1939, 254 cases of carcinoma of the large bowel (including 2 of the appendix and 10 of the anus) were seen at the University of Maryland Hospital. Approximately 97 per cent of the cases were followed up.

Of the 242 cases of adenocarcinoma of the colon and rectum 79, or 33 per cent, were operable. This is a low operability and is partly explained by the fact that 56 cases were considered inoperable in which there were no metastases. They were judged inoperable on account of the extent of the tumor.

Among the 79 cases operated on there were 30, or 38 per cent, of operative deaths. Peritonitis was the cause of death in 18, or 60 per cent of the cases. Twenty-four of the patients have survived three years or more. One patient has recurrence after fifteen years. This is probably another tumor. Of the 25 remaining cases 14 have died and 11 are still living, having survived varying periods less than three years. Two of these have liver metastases.

Of the 163 inoperable cases, aside from 3 survivals of fourteen years, thirteen years and six years under electrocoagulation and radium, and 1 survival of four and one-half years under radium alone, there were no survivals of over three years and the average survival was fifteen months.

Thirty-six patients were treated with radium. All of the three long-term survivals mentioned above were Grade III tumors. Dukes' classification was used, according to which A indicates that the tumor is limited to the mucosa and submucosa, B indicates involvement of the muscularis and C peritoneal or regional node involvement. The survival of one inoperable patient for fourteen years casts some doubt on the criteria of inoperability adopted.

Operation should be performed whenever possible as the chance of survival in untreated cases is poor, while if adequate excision is performed and the patient survives the operation his chances for survival are good.—*Audrey G. Morgan.*

BUIRGE, RAYMOND E. Carcinoma of the large intestine. *Arch. Surg.*, May, 1941, *42*, 801–818.

This article is based on 416 cases of malignant tumor of the large intestine found among 26,798 autopsy records at the University of Minnesota from 1910 to 1937. The percentage of male to female patients was 1.77 to 1; their average age was fifty years, six months. The most frequent sites of the cancer were the rectum, the sigmoid flexure and the cecum.

There are no specific symptoms early in the disease. Generally the patient does not come for treatment until hemorrhage or signs of obstruction develop. A part of the blame for failure to come earlier for treatment rests on the patient himself and part of it on the general practitioner to whom he first goes for advice. Not only should the public be educated in regard to the early signs of cancer, but the family physician should be trained in early diagnosis and treatment. If symptoms such as melena, changes in intestinal habit, diarrhea or constipation or alternation of the two, weakness, anemia, loss of weight or signs of intestinal obstruction appear, complete clinical and roentgen examination should be made at once. Roentgen examination is absolutely indispensable for the early diagnosis of cancer of the colon. Among 97 diagnoses based on roentgen studies of the colon, 85 per cent were correct. Digital examination of the rectum and the use of the sigmoidoscope are useful aids in the diagnosis of cancer of the distal part of the colon.

The most frequent mistaken diagnoses made in cancer of the colon are discussed and the suggestion made that the trainees in cancer clinics should carefully correlate the histological and clinical findings in all cases. Such a study carried out in all cancer institutes over a period of five years would give invaluable information.—*Audrey G. Morgan.*

MACDONALD, DEAN. Common bile duct peristalsis; preliminary report. *Surg., Gynec. & Obst.*, Dec., 1941, *73*, 864–866.

A case is described in which roentgenoscopic examination of a pathological common bile duct showed clear evidence of peristalsis of the duct. Cholangiograms are given showing the evidence on which this conclusion was based. There were changes in the internal diameter of the duct which could have been caused only by irritation by the tube, contraction of the sphincter muscle or peristalsis. Irritation could not produce such changes if there was not an inherent ability to contract and relax. The constriction was 1 inch from the end of the duct and sphincter tissue rarely extends so far up.

Peristalsis should be expected in the common duct because it is an integral part of the bile tract and an uninterrupted flow of bile is necessary to good health.

The clinical conclusion to be drawn from this finding is that serial cholangiograms should be taken, as the findings on a single plate may be misleading.—*Audrey G. Morgan.*

FELDMAN, MAURICE. The terminal common bile duct and duodenal papilla; roentgenological consideration. *Surg., Gynec. & Obst.*, Dec., 1941, *73*, 838–844.

Little attention has been paid in the roentgenological literature to the changes in the terminal common bile duct and the papilla of the duodenum. Of course a knowledge of the normal roentgen appearance of this part of the digestive tract is a necessary prerequisite to an interpretation of pathological changes.

The author has previously published a description of the normal roentgen appearance of the ampullary portion of the duodenum and in this article he describes and illustrates with roentgenograms pathological changes in this area which may be of diagnostic significance, including enlargement and broadening of the plica longitudinalis duodeni fold, encroachment of the enlarged duodenal fold on the lumen of the duodenum, mucosal changes surrounding the longitudinal fold and changes in the pattern of the mucosa of the ampulla, enlargement of the major duodenal papilla, filling defect in the outline of the duodenum, varying degrees of stenosis, defect from secondary ulceration, invasion of the pancreas by carcinoma, which may cause signs of pressure on the duodenum, cholecystographic changes which cause nonfilling of the gallbladder when the bile duct is occluded and pressure defect of the stomach in late cases.—*Audrey G. Morgan.*

ARCE, JOSÉ. Hydatid cyst of the liver. *Arch. Surg.*, June, 1941, *42*, 973–987.

The surgical treatment of hydatid cyst of the liver is discussed and illustrations given showing the technique of the different operations used: midline laparotomy, high laparotomy, transdiaphragmatic parapleural laparotomy

and transpleural transdiaphragmatic thoracolaparotomy. The author uses his own incision, called in Argentina Arce's gridiron transverse laparotomy, for all surgical conditions of the biliary system and the right lobe of the liver, including hydatid cysts. This is simply McBurney's gridiron incision for appendectomy used in the upper part of the abdomen.

When the cyst has been reached it can be treated by removal of the parasite, followed by suture of the adventitia without drainage, removal of the parasite followed by marsupialization and drainage of the adventitia, removal of the parasite without suturing or draining the adventitia, or total removal of the cyst.

Roentgenograms are given of cysts in different parts of the liver and the indications for the various types of operation discussed. Sometimes the roentgenogram shows calcification of the adventitia. If such a cyst is not too large or too far from the periphery of the organ it should be totally removed. Marsupialization should be used for cysts opening into the biliary tract or into a bronchus.—*Audrey G. Morgan.*

SKELETAL SYSTEM

Lachman, Ernest. The limitations of the roentgen diagnosis of fractures. *Surg., Gynec. & Obst.*, Aug., 1941, *73*, 140–151.

Since roentgen rays have been used in medicine the opinion seems to have become established that the roentgen report of a fracture is something absolutely objective and definite and not subject to errors of interpretation.

The author points out that this is by no means true and that there are very definite limitations to the accuracy of roentgen diagnosis of fractures. In order for a physician to interpret roentgen findings correctly he must know the laws of roentgen physics, particularly those of projective geometry. He must know the normal roentgen anatomy of the skeleton at different ages and the roentgen symptomatology of bone diseases and must take into consideration the possibility of supernumerary bones and other abnormalities that may simulate fracture.

Sometimes the patient is so severely injured that it is impossible to make roentgenograms in all the projections necessary for roentgen diagnosis. It may not be possible to visualize a fracture line in cartilage or because it is too minute to be shown. The projections used may not be chosen properly to show the fracture in question. Complex parts of the skeleton, such as the skull and vertebrae, are apt not to be shown because of superimposition of other bones or parts of bones. And in cases of multiple fracture some of the fractures may not be included in the roentgenogram.

Special care is necessary in evaluating the displacement of fragments. Angulation of fragments toward or away from the plane of the roentgen film may cause misinterpretation. The introduction of the lateral projection has decidedly influenced the diagnosis and treatment of fractures of the neck of the femur, and doubtless further technical improvements will overcome others of the limitations in the roentgen diagnosis of fracture. But the physician and roentgenologist must recognize the existence of such limitations.

None of the signs of healing of fracture are absolute. A fracture line may be masked for instance by exuberant callus. The clinical findings must be considered in evaluating bone repair. The roentgen signs of fracture may disappear so completely that it is impossible to say that there has ever been a fracture. This may be of importance in medicolegal cases, as may the fact that after about a year it is impossible to judge the date of a fracture from the roentgenogram.—*Audrey G. Morgan.*

Riesenman, F. Regis, and Yater, Wallace M. Osteogenesis imperfecta; its incidence and manifestations in seven families. *Arch. Int. Med.*, May, 1941, *67*, 950–967.

Seven white families living near Washington, D. C. were studied, and 91 cases of osteogenesis imperfecta were discovered among their 255 members. Four of the families are described in detail and family trees given showing the incidence of the disease.

The triad of symptoms in this disease is blue sclerotics, occurring in 100 per cent of the cases, brittle bones with multiple fractures in 65 per cent and otosclerosis with progressive deafness in 43 per cent. The roentgenogram shows the bones of the extremities very slender with greatly expanded ends. There are peculiar cross striations. The bone is very dense and hard and looks and cuts like marble.

The disease is evidently due to a hereditary inferiority of the mesenchyme and it is possible that improvement in its treatment may be brought about by a more complete knowledge of genetics and eugenics. There is no proof that

the endocrine system is involved or mineral metabolism affected.

The disease may develop during intrauterine life and the child may have multiple fractures at birth. This form is rare. All the cases in this series belonged to the post-natal or infantile type. These children have blue scleras at birth.

There is no specific treatment. Early orthopedic treatment may be useful in preventing crippling. The use of thymus extract has been recommended because of the influence of the thymus on the growth and development of bone. But it has generally not been given until the child has had several fractures. It would be more logical to give it to the mother during pregnancy in affected families, and to begin its administration at once to any child born with blue scleras.—*Audrey G. Morgan.*

COUCH, J. H., and ROBERTSON, H. F. Occurrence of postoperative acidosis and pagetoid bone changes in hyperparathyroidism. *Surg., Gynec. & Obst.*, August, 1941, *73*, 165–174.

Two cases of parathyroid tumor associated with hyperparathyroidism are described which illustrate two different aspects of the condition. The first case was in a woman of fifty-two who first presented the signs of hypercalcemia and then of multiple bone cysts due to decalcification. A diagnosis of hyperparathyroidism was made and the tumor removed by operation. Ten hours after operation a severe acidosis developed. The danger of such postoperative acidosis in this condition should be borne in mind. It is probably caused by the retention in the blood of acid radicals, such as sulphates, phosphates and chlorides, while sodium is excreted freely by the kidneys and calcium is retained in the bones. The basic radicals are depleted and acidosis occurs. This same mechanism may cause hypocalcemic tetany. Either of these conditions may be fatal. The acidosis was successfully treated in this case by giving sodium bicarbonate intravenously. A salt-free diet for a week or so before parathyroidectomy would be a typical preventive measure in these cases.

In the second case in a woman of sixty-four the roentgenogram showed bone changes resembling those of Paget's disease. The changes were probably caused by alternate exacerbations and remissions of parathyroid activity which brought about alternate periods of decalcification and recalcification of bone.—*Audrey G. Morgan.*

BATTS, MARTIN. Periosteal fibrosarcoma. *Arch. Surg.*, March, 1941, *42*, 566–576.

Periosteal fibrosarcoma is an unusual type of tumor. In a series of 200 primary malignant bone tumors seen at the University Hospital, Ann Arbor, Mich., 27 were of this type. About two-thirds of the patients were males and 21 of them, or 78 per cent, were less than forty years of age. According to the histories neither heredity nor trauma played any important part in causing the tumor.

The average duration of symptoms was twenty months, which is relatively long as compared with other malignant bone tumors. The commonest symptoms were pain and swelling. In 3 cases there was tumor formation without any history of pain. The tumors were deep-seated, smooth and not fixed to the overlying tissues, but they were relatively immobile because of firm fixation to the periosteum.

Roentgen examination showed two types of changes, destructive and reactive. Roentgenograms showing these types of change are given. Destructive changes were more frequent than reactive ones. The histopathological findings were essentially the same as those seen in any sarcoma originating from fibrous tissue.

The tumors were divided into four grades according to the degree of malignancy. Tables are given showing the percentage of five year survivals, as based on site of tumor, type of treatment and degree of malignancy. They indicate that the most important factor in prognosis is the degree of malignancy. All of the cases of Stage I showed five year survival, 70 per cent of those of Stage II and none of those of Stages III and IV. The site of the tumor apparently does not affect prognosis and the type of treatment was a less decisive factor than the degree of malignancy. Local excision plus roentgen therapy gave the highest percentage of five year survival.

Follow-up studies were made in 25, or 93 per cent, of the cases. Ten patients, or 40 per cent, had survived for more than five years after treatment. Three of the patients died of malignancy more than five years after treatment, showing that five year survival does not mean cure. Most of the deaths, 13 or 52 per cent, were from metastases in the lungs.—*Audrey G. Morgan.*

Badgley, Carl E., and Batts, Martin, Jr. Osteogenic sarcoma. *Arch. Surg.*, Oct., 1941, *43*, 541–550.

Osteogenic sarcoma is the most common type of primary malignant bone tumor, constituting almost half of the total number of bone tumors reported by the American Registry of Bone Tumors. At the University Hospital, Ann Arbor, Mich., a series of 80 cases treated from 1925 to 1938 has been studied. In half of these cases the patients were in the second decade of life. The average age on admission was twenty-nine years, the youngest patient was eight years of age, the oldest seventy-two. Sixty-four per cent of the patients were men and 36 per cent women. There was a family history of tumor in only 13 per cent of the cases and a history of trauma in about a third of them.

The average duration of symptoms from onset to time of admission was thirteen months. The chief symptoms were pain and swelling, the pain preceding the swelling in the majority of cases. In almost all the cases the patients were in good health when the symptoms began. There was a palpable tumor in 73 cases, or 91 per cent, which was hard and moderately tender. The regional lymph nodes were enlarged in only 2 of the cases. A few of the patients had a low-grade fever.

The lesions occurred most frequently in the ends of the long bones and in half of this series of cases they were at or near the knee joint.

The treatment of choice in this series was radical amputation, generally not preceded by irradiation. When roentgen treatment was given after operation it was generally as a palliative measure, usually for lung metastases. If amputation was impossible local excision was performed, generally followed by roentgen treatment.

Follow-up studies showed that 63 per cent of the patients had died. Of the other 17 one had metastases and the others were well. There were 15 five year survivals, or 19 per cent, and 4 ten year survivals, or 5 per cent. One patient was alive and well fourteen years and seven months after a mid-thigh amputation. The average survival in the cases of death was thirty-one months. That even a ten year survival does not necessarily mean cure is shown by the fact that one patient died of pulmonary metastases that developed thirteen years after a mid-thigh amputation.

Prognosis is better in older patients than in younger ones, in cases in which symptoms appeared relatively late, in distal than in central lesions of the extremities and in the more highly differentiated types of tumor. The longer the survival after operation, the more favorable the prognosis.

It has not been proved that biopsy endangers the patient's life, though in this series the average period of survival in cases in which biopsy had been done was twenty-eight months, and in those in which it was not done thirty-five months.—*Audrey G. Morgan.*

GENERAL

Campbell, Darrell A. Carcinoma of the upper extremity. *Arch. Surg.*, Nov., 1941, *43*, 803–810.

Carcinoma of the upper extremity is not common. It constitutes less than 10 per cent of all carcinoma.

A series of 36 cases treated at the University Hospital, Ann Arbor, Mich., is discussed. The most frequent etiological factor was carcinomatous change occurring in keratoses. These carcinomata frequently develop in the scars of old burns and in the early days of the use of roentgen rays they often developed after roentgen and radium irradiation. Lupus vulgaris is a common etiological factor.

In this series of cases 32 of the patients were men and 4 women. Wide surgical removal of the lesion and irradiation of the site and of the regional glands proved the best treatment. Only 4 of the patients, or 11 per cent, survived five years or more without recurrence. But a considerable number died of intercurrent disease before the end of the five year period was reached, and if these and the patients who have not yet reached the end of the five year period are counted the percentage of cures becomes seventy-two. In half the cases there were unrelated tumors of other parts of the body.

Although 15 of the patients have died, only 7 died directly of the carcinoma. The others died of intercurrent disease. The average of those who died from carcinoma was 52.7 years and of those who died from intercurrent disease seventy-five years.—*Audrey G. Morgan.*

Camiel, Mortimer R., and Bolker, Herman. Carcinoma erysipelatodes; subepidermal lymphatic metastases confused with opera-

tive sequelae. *Surg., Gynec. & Obst.*, March, 1941, *72*, 635–641.

Unna noticed the resemblance of certain tumor metastases to erysipelas. This condition was first named erysipelas carcinomatosa in 1924 by Kuettner, but Rasch in 1931 criticized this name and suggested that of carcinoma erysipelatodes because the condition is primarily cancerous.

The authors describe 2 cases which occurred after operation and roentgen treatment for carcinoma of the breast in women forty-seven and forty-eight years of age. The reddened area which developed around the operation scar was in both cases interpreted as postoperative inflammation or radiodermatitis. Such a severe dermatitis caused by irradiation would, of course, be of medicolegal importance. A study of histological sections in both cases, however, showed that the lesions were cancerous.

More than 200 serial sections were studied in an effort to determine whether the metastasis had been disseminated through the blood or lymphatic channels. Apparently it had been through the subepidermal lymphatics and tissue spaces rather than through the veins, as no erythrocytes were found in the vessels that contained the tumor cells. This is a chronic and not an acute process and the well demarcated, reddened and advancing border is the only feature that it has in common with erysipelas.—*Audrey G. Morgan.*

SAPHIR, OTTO, and PARKER, MORRIS L. Metastasis of primary carcinoma of the breast; with special reference to spleen, adrenal glands and ovaries. *Arch. Surg.*, June, 1941, *42*, 1003–1018.

There is very little definite information in the literature in regard to metastases from cancer of the breast. The authors therefore thought it worth while to report the pathological findings in 43 cases from the Michael Reese Hospital. The commonest site of metastases was in the lungs which were involved in 28 cases, and next the liver in 24 cases. This was followed by involvement of the adrenal glands in 19 cases, the spleen in 10 cases and the ovaries in 7 cases. It has been said that carcinoma of the spleen secondary to cancer of the breast is part of a generalized microscopic carcinomatosis. In 3 of the cases there were no metastases.

A table is given showing the period of survival after operation. It is evident that neither the length of life nor the spread and number of metastases is dependent on the type of carcinoma. But a high degree of malignancy is indicated by the breaking down of the lining of the gland structures and the dissemination of isolated tumor cells in the surrounding breast tissue. Most of the tumors which caused metastases in the spleen, ovaries and adrenal glands showed an infiltration of isolated carcinoma cells outside the primary tumor. This was particularly true of the signet ring cell variety of mucinous carcinoma.

With reference to treatment, in this series of cases the results were no better when irradiation was given following operation than when it was not. This would seem to indicate that irradiation is not effective for metastases. But the number was small and the tumors particularly malignant, so that no definite conclusions can be drawn in regard to this point.—*Audrey G. Morgan.*

BRAUND, RALPH R., and MARTIN, HAYES E. Distant metastasis in cancer of the upper respiratory and alimentary tracts. *Surg., Gynec. & Obst.*, July, 1941, *73*, 63–71.

It is well known that the regional lymph nodes are very frequently involved in cancer of the upper respiratory and intestinal tracts but very little has been written about systemic metastases from these tumors.

The records of the Memorial Hospital in New York show autopsies on 308 patients who died of cancer in these locations. Histological examination of the primary tumor was made in 284 of the cases which are considered in this article. They are divided into tumors of the lip, mucosa of the cheek, floor of the mouth, gums, tongue, palate, tonsil, nasal cavity and sinuses, wall of the pharynx, extrinsic and intrinsic larynx and esophagus. Tables are given showing the incidence of distant metastases from these different sites, the distribution of the distant metastases and the relationship of the duration of the disease to the occurrence of distant metastases.

The lowest incidence of distant metastases was from tumors of the floor of the mouth, 6.2 per cent, and the highest from those of the nasal cavity and sinuses, 35.7 per cent. Of the whole 284 cases, 23.2 per cent showed distant metastases. These were blood-borne metastases. The most frequent metastases were in the lungs, liver and pleura, which showed 35, 24 and 18 cases of metastasis respectively.

It is generally believed that cancer of the aged is comparatively benign while in the young it is particularly malignant. This belief was not confirmed by these cases, though the 66 patients with visceral metastases showed an average age of 55.8 years while the average age of the patients without visceral metastasis was 59.4 years. Syphilis seemed to have no causal significance in the production of distant metastases. Only 3 of these patients had syphilis.

Only the groups with cancer of the mucosa of the cheek and of the esophagus showed a higher incidence of visceral metastasis with a longer history of disease before treatment. In the other groups there was a shorter history from onset to treatment in the cases with distant metastases.

The morphology of the tumor was of little value in determining the probability of distant metastasis. Among the patients with epidermoid carcinoma none had visceral metastases who had not at some time during the course of the disease shown involvement of the cervical lymph nodes, but 2 patients with adenocarcinoma of the palate had visceral metastases not preceded by lymph node involvement.—*Audrey G. Morgan.*

List, Carl F. Intraspinal epidermoids, dermoids, and dermal sinuses. *Surg., Gynec. & Obst.*, Oct., 1941, *73*, 525–538.

Epidermoids, dermoids and dermal sinuses are structures that contain elements of the skin. They are dysembryonic malformations rather than true tumors, but are called tumors here because of their tendency to expand. Epidermoids are made up of the superficial layers of the skin, dermoids contain all layers of the skin and also its accessory organs, such as sweat and sebaceous glands and hair follicles. Dermoid sinuses are tubular structures in direct connection with the skin. The embryological theories in regard to their origin are discussed.

The author describes and illustrates with roentgenograms 5 cases of his own which brought the total number of cases at the time of the writing of his article up to 56. Since then he has had another case and 4 more have appeared in the literature, making a total of 61. These tumors are in the majority of cases below the 12th dorsal vertebra and many of them are in the cauda equina. Only 1 case has been described in the cervical cord. Almost two-thirds of all the lesions were within the leptomeninges, one-fifth were frankly intramedullary and only a few extradural. Most of the lesions were on the posterior surface of the cord.

No matter at what age they become manifest these tumors are present, though latent, at birth. Epidermoids and dermoids show a tendency to long remissions. The neurological symptoms and spinal fluid findings are about the same as in other slowly growing tumors of the spinal cord. The total protein in the spinal fluid does not reach the very high levels that it does in neurinomas.

As these are benign encapsulated tumors their surgical removal should be simple, but results have not been good until the past fifteen years. Total removal may be impossible because of firm adherence of the capsule to the cord and nerve roots. And in intramedullary cases it may be impossible to remove the whole tumor without injuring the cord. But even intracapsular enucleation with partial removal may bring about improvement for a long time. Dermal sinuses should be totally excised. If the sinus is infected the results are improved by the use of sulfanilamide, sulfathiazole and similar drugs.—*Audrey G. Morgan.*

Donhauser, J. Lewi, and de Rouville, William H. Multiple myeloma, with special reference to soft tissue metastasis. *Arch. Surg.*, Dec., 1941, *43*, 946–1020.

Multiple myeloma is a primary malignant tumor of bone marrow with multiple foci in the bones. It is usually associated with anemia and Bence-Jones proteinuria. Treatment is hopeless and death generally occurs within two years. This form of tumor generally develops in the sixth decade of life with the peak at fifty-five. As it most frequently involves the bones that contain the most red marrow it is commonest in the vertebrae, ribs, sternum, clavicle and skull, though any of the bones may become involved. The tumor is very vascular and more or less gelatinous. It is definitely destructive of bone and there is no evidence of bone repair. Spontaneous fractures are very frequent. Soft tissue may become involved also, particularly the blood-forming tissues. The only change in the blood may be anemia, but in most cases there is an increase of lymphocytes and the myelocytes often increase to 10 per cent.

In any patient who complains of backache or obscure pain in the bones, especially if he is in the sixth decade of life, myeloma should be suspected. The disease is so rare that often physi-

cians do not suspect it and many mistaken diagnoses are made. When it is suspected the pathologist, chemist and roentgenologist should be called in for confirmation of the diagnosis. The chemist should make complete examinations of the urine with regard to specific gravity, presence or absence of albumin and sugar, the calcium content and the presence of Bence-Jones protein. Determinations of blood calcium, phosphorus, phosphatase, total protein, including albumin-globulin ratio, non-protein nitrogen, creatinine, urea and uric acid should be made.

Roentgen examination must be made by a roentgenologist who can detect very slight differences in the density of bone. The most characteristic finding is decreased density of the affected bones with absorption and replacement of lime salts by tumor tissue. There are usually sharply punched-out holes in the bones. These are seen in a number of other conditions, however, which must be ruled out by exclusion. There is no compensating hyperostosis.

Five cases are described in detail and illustrated with roentgenograms and photomicrographs. Though it has been claimed that metastases are rare or non-existent in this disease there were metastases in 3 of these 5 cases. There was widespread direct extension of the disease in one case. In 3 of the cases there was Bence-Jones protein in the urine. The urinary findings were inconstant. In 4 of the cases severe pain in the back was the first symptom. There was low blood pressure in 2 of the cases but this is not a pathognomonic symptom.—*Audrey G. Morgan.*

LUTZ, J. FLETCHER. Calcinosis universalis. *Ann. Int. Med.*, Jan., 1941, *14*, 1270–1282.

Calcinosis universalis is a definite disease entity characterized by the deposition of calcium in the subcutaneous tissue, muscles and sometimes along the nerve trunks. There are none of the abnormalities which usually cause pathological calcification, such as chronic inflammation, infarction, hemorrhage or tissue necrosis. Blood calcium is normal in the majority of cases, most of which are associated with scleroderma. Diagnosis is readily made by roentgen examination which shows the calcium deposits throughout the subcutaneous tissue. There is no evidence of bone involvement such as is seen in parathyroid disease. The patient's general health may be affected by the mechanical disturbance resulting from the stiffening of the muscles.

Prognosis is unfavorable as to cure. There is no known effective treatment. The disease is slowly progressive but does not generally cause death. In the one case in which autopsy has been reported the patient died of an intercurrent disease. No changes were found in the parathyroids, though the patient had had the disease for thirty-seven years.

A case is described in a schoolgirl sixteen years of age in whom a fistula of the left hip developed after a fall on the hip. Biopsy and chemical examination showed a rich deposit of calcium salts, mostly phosphate, in the muscle fascia and superficial layers of muscle tissue of the leg but no true ossification, and no neoplastic bone formation. Roentgenograms and a photomicrograph of the histological findings are given.—*Audrey G. Morgan.*

ROENTGEN AND RADIUM THERAPY

WALLACE, WILLIAM S. Studies in radiation sickness. II. Vitamins B_1 and C and the small intestinal change in radiation sickness. *South. M. J.*, Feb., 1941, *34*, 170–173.

The author describes the technique of irradiation for carcinoma of the cervix used at Duke Hospital, and the treatment of these patients with vitamins B_1 and C in an effort to prevent radiation sickness.

The patients treated with vitamin B_1 were given daily intramuscular injections of 10 mg. synthetic thiamin chloride, corresponding to 3,000 international units. Those treated with vitamin C were given daily doses of 50 mg., or 1,000 international units, of sodium ascorbic acid in the form of "cevalin." These were large doses and it is improbable that larger ones would have had any further effect.

These vitamins almost completely eliminated the severe nausea and vomiting of radiation sickness and the patients were more comfortable subjectively, but they had no effect on the diarrhea and did not prevent the changes in the ileum seen after heavy irradiation. These changes resemble those of deficiency states, but they are evidently not caused by lack of vitamins B_1 and C.

In the discussion Dr. Keith said that he believed the dosage of 300 r per day over two fields reported in this paper was quite high, even though 200 kv. was used. Whenever 300 r a day

is given over the abdomen it causes some nausea. With high voltage and high filtration he usually does not give more than 200 r per day. He has had more relief from radiation sickness from nicotinic acid than anything else, 50 mg. in a glass of water thirty minutes before meals.

The importance of the psychic factor in radiation sickness was mentioned.—*Audrey G. Morgan.*

Daland, Ernest M. Radiation damage to tissue and its repair. *Surg., Gynec. & Obst.*, Feb. 15, 1941, *72*, 372–383.

In the early period of the use of roentgen rays much damage was done because of lack of accurate knowledge of the action of the rays and of means for protection. Now with more adequate protection damage is less but still occurs.

It may be early, in the form of erythema and ulceration or late in the form of degenerative changes in the tissues and possibly the development of cancer in irradiated areas. Infection in a heavily irradiated area may cause necrosis and sloughing. The mucous membrane of neighboring organs may be almost as sensitive to irradiation as the tumor itself and serious damage may be due to this cause. Considerable damage has been done by a method of removal of superfluous hair by beauty parlors in use some years ago. It was really a roentgen treatment and without knowledge of dosage on the part of the operators, the results were serious in many cases.

Irradiation of a region does greater harm if the circulation is poor. Often the circulation in the extremities is not good and as a result they do not bear irradiation as well as more vascular parts of the body. Circulation is poorer after irradiation and if an artery supplying an area damaged in this way is ligated later on surgical operation necrosis of the whole area may occur.

Cancer may develop in an irradiated area after varying intervals. The shortest interval seen by the author between irradiation and the development of cancer was two and one-half years, the longest eighteen years. Roentgen cancer is usually of the epidermoid type. Metastasis begins late but when it does begin it extends rapidly, first through the lymphatics and then through the blood. Twenty-five cases of various types of injury from roentgen irradiation are described and illustrated with photographs —*Audrey G. Morgan.*

Young, Forrest. The treatment of persistent recurrent basal cell carcinoma of the face. *Surg., Gynec. & Obst.*, August, 1941, *73*, 152–164.

Basal cell carcinoma usually occurs on exposed areas, such as the face. It is comparatively easy of cure either by irradiation, cautery or electrocoagulation. Sometimes, however, the initial treatment is inadequate and there is persistent recurrence, which may make this a very serious condition.

If the growth recurs radical removal must be performed even if disfigurement results. The physician or surgeon is often hesitant in treating these cases because of the fear of causing disfigurement. But often the tumor extends under apparently normal skin and care must be taken to excise well beyond the limits of the lesion. Surgery is preferable to irradiation at this stage. The author believes repair should be done immediately rather than after an interval of twelve to eighteen months as has often been advocated. If grafting is necessary the flap can be prepared before the operation and applied immediately after it. If it is a pedicled flap the pedicle can be cut some four to six weeks later. This method requires a minimum of hospitalization.

Six cases treated in his way are described in detail and illustrated with roentgenograms.—*Audrey G. Morgan.*

Arbuckle, Millard F., and Stutsman, A. C. Pharyngeal and laryngopharyngeal cancer; a new combination of surgery and radiation therapy in their treatment. *South. M. J.*, Feb., 1941, *34*, 219–221.

Four cases are reported in which the authors removed the normal thyroid and epiglottic cartilages before radiotherapy was given. This was done because in these cases, even when the tumor is destroyed by irradiation, the cartilage becomes edematous and finally breaks down.

In the discussion Dr. Le Jeune said that he had had poor results from irradiation in laryngeal cancer. He had had no experience with removal of the laryngeal cartilage, but if irradiation does not help the metastatic glands he could not see how it would help lesions inside the larynx if the cartilage was removed. If irradiation is effective it would be of special value in tumors of the pyriform fossa or the hypopharyngeal area which are not accessible to operation.

Dr. Arbuckle replied that he did not know whether their method would be found an improvement but that any method which promised improvement was worth trying, as the mortality in these cases, except in genuine cordal cancer, is still distressingly high. He believes surgery is indicated in operable cases, but irradiation alone or in combination with surgery, should be used in cases in which the location makes it difficult or impossible to remove all of the tumor by surgery.—*Audrey G. Morgan.*

RHINEHART, D. A., and RHINEHART, B. A. Protracted roentgen treatment of malignancies particularly of the head and face. *South. M. J.*, August, 1941, *34*, 820–823.

The fundamental principles of Coutard's protracted fractional method of roentgen therapy are high voltage, heavy filtration, low intensity, long single exposures, long treatment time and high total dosage. There are many modifications of the treatment. The technical factors most frequently used are: 200 to 220 kv., 5 to 25 ma., a distance of 50 to 70 cm., filtration from 0.75 to 2 mm. copper and 1 to 2 mm. aluminum and a daily dose of 200 to 250 roentgens, measured in air. Often a composite filter of 0.4 mm. tin plus 0.25 mm. copper plus 1.0 mm. aluminum is used instead of the pure copper. It gives a beam equivalent in quality to that of more than 2 mm. copper but at a greater intensity, so that treatment time is shortened.

Because of the high total dosage given, up to 6,000 to 8,000 r, the reactions are apt to be severe. It is a treatment that is hard for both patient and physician.

It is used chiefly for tumors of the mouth, pharynx, larynx, tongue and tonsils. A table is given showing the results in 61 cases. Thirty-two of the patients are dead, 29 of them of the original disease. Twenty-five are living, 20 of them apparently free of cancer. Treatment has been satisfactory in 23 cases, or 37.7 per cent.—*Audrey G. Morgan.*

NEW, GORDON B., and HALLBERG, O. ERIK. The end-results of the treatment of malignant tumors of the palate. *Surg., Gynec. & Obst.*, 1941, *73*, 520–524.

The authors review 173 cases of malignant tumors of the palate treated at the Mayo Clinic from 1907 to 1939. During this time 236 cases of benign tumor of the palate were seen.

The most frequent tumors at this site are adenocarcinoma of the mixed type (76 cases in this series) and squamous cell epithelioma (84 cases in this series).

Among the cases of adenocarcinoma of the mixed type the average age of the patients was fifty years for males and forty-two years for females. The average duration of symptoms was 4.75 years, the shortest one month and the longest thirty years. In almost half the cases the tumor was at the junction of the hard and soft palates, which is the chief location of the openings of the ducts of the mucous glands. These tumors can generally be diagnosed easily from the location, the long duration and the movable, hard, nodular tumor. Fibromas or fibrosarcomas are the only tumors that may be confused with them.

These tumors are removed surgically whenever possible. If it is doubtful whether the whole tumor has been removed, radium seeds or needles are used at the time of operation. In all but one of the cases here reported the tumor was removed through the mouth. The lymph nodes of the neck were not removed unless they showed metastases. Generally these tumors do not metastasize. In 7 cases irradiation had been used before the patients came to the Clinic and the tumors were inoperable. In these cases only irradiation was used. The number of five year survivals was 46, or 88 per cent of the patients traced. There were 29 ten year survivals, or 78 per cent of the 37 patients traced. This shows that these tumors were not very malignant.

Among the 84 patients with squamous cell epithelioma the average age was 58.2 years; 10.7 per cent of the patients were women. The preferred treatment was removal by surgical diathermy under intratracheal nitrous oxide-oxygen anesthesia or intravenous pentothal sodium. The number of five year survivals was 20, or 38 per cent of the 52 patients traced. Five year survival in cases of Grade I was 100 per cent, Grade II, 44 per cent, Grade III, 38 per cent, and Grade IV none.

The other 13 cases were made up of 3 of melanoepithelioma, 4 of fibrosarcoma, 1 each of fibromyxosarcoma, myxosarcoma and chondrosarcoma and 3 of lymphosarcoma.

Among the cases of melanoepithelioma there were two survivals of four and two years. The other patient was given only palliative irradiation. The 4 patients with fibrosarcoma showed freedom from recurrence after five, ten and

twenty years. Only palliative irradiation was used in the fourth case. The patient with fibromyxosarcoma was treated with radium but died two years later. The patient with myxosarcoma died a month after treatment. The one with chondrosarcoma had had a tumor of the palate removed ten years before admission to the Clinic. She was in very bad condition on admission and only palliative roentgen irradiation was used. All of the 3 patients with lymphosarcoma had palpable lymph nodes when examined. They were all given palliative roentgen treatment but all of them died within eleven months of generalized metastases.—*Audrey G. Morgan.*

Kamperman, George. The present status of treatment of gynecological cancer; with special reference to results obtained since introduction of supervoltage roentgen therapy. *Surg., Gynec. & Obst.*, Feb. 15, 1941, *72*, 384–390.

This article reviews the 845 cases of gynecological cancer treated at Harper Hospital, Detroit, Mich., from 1922 to 1935 on the basis of the five and ten year survival figures. They include 636 cases of cancer of the cervix, 77 of cancer of the fundus, 171 of cancer of the ovary and 31 of cancer of the external genitalia.

Tables are given showing the results in these groups. Only survivals were counted. All patients who died were assumed to have died of cancer and those lost sight of were also counted as dead of cancer, though some of them doubtless survived. Therefore the survival figures given are the lowest possible.

At first treatment was with 200 kv. constant potential, 1 mm. copper filter, but in 1933 supervoltage roentgen treatment was instituted with 500 to 600 kv. constant potential, 7 mm. copper filter. Only cases that were inoperable and in which intrauterine radium treatment could not be given were treated with roentgen irradiation alone. Improvement in the survival curves since the introduction of supervoltage therapy indicates that it does give better results than earlier methods.

In carcinoma of the cervix in the earlier years operation was performed in operable cases, followed by irradiation. Since 1928 the intrauterine use of radium has been relied on chiefly, the largest tolerance dose being given—a total dosage of 7,200 to 10,000 milligram-hours. Roentgen rays are used to irradiate areas around the periphery of the pelvis outside the action of the radium. From 1922 to 1928 the five and ten year survivals averaged 16 and 12 per cent, from 1928 to 1933, 21 and 15 per cent, and from the introduction of supervoltage therapy to 1935 the five year survivals reached 35 per cent.

In carcinoma of the uterine fundus preliminary treatment with intrauterine radium and roentgen rays is given, followed in six to ten weeks by operation. This increased five year survivals to 71 per cent as compared with 55 per cent in the period when operation was performed first. The absolute five year survivals since the introduction of supervoltage average 50 per cent.

The curves for five and ten year survival in carcinoma of the ovary are 20 and 18 per cent for the whole time. Supervoltage roentgen therapy did not bring about any improvement in this group.

Treatment must be strictly individualized in carcinoma of the external genitalia. The five year survivals for the whole period average about 16 per cent and the ten year survivals almost the same.—*Audrey G. Morgan.*

MISCELLANEOUS

Hames, Fred. Accurate placement of radon seed by suture method. *South. M. J.*, May, 1941, *34*, 462–464.

In the ordinary methods of using radon seeds they tend to bunch together in a dependent part because of the heaviness of the gold. This may causes radiation necrosis of bone.

The author describes a method by which one to twenty radon seeds with gold walls 0.3 mm. thick can be applied in one piece of material. The method cannot be used for radium. The material is a woven silk structure with openings 1 cm. apart for the seeds. As it is woven the opening closes after the seed is inserted. Each piece of material is fitted with a small metal collar into which the needle is screwed so that the suture can be placed without having to pass it through the tissue doubled. After it is placed it is fastened at each end by crushing a hollow lead shot over a threaded glass bead. After the radiation has been given the suture holding the seed can be removed as simply as removing a capillary drain. The seed can be recovered by burning away the silk material.

The method is simple and easy to apply, it prevents radiation necrosis of bone, reduces secondary rays and makes the patient more comfortable, as he can empty his mouth and take food and drink.—*Audrey G. Morgan.*

ERF, L. A. and LAWRENCE, J. H. Clinical studies with the aid of radio-phosphorus. III. The absorption and distribution of radiophosphorus in the blood of, its excretion by, and its therapeutic effect on, patients with polycythemia. *Ann. Int. Med.*, Aug., 1941, *15*, 276–290.

Four robust workmen with recently healed fractures and 6 patients with polycythemia were examined to determine the amount of radiophosphorus retained by various fractions of the blood, to determine the amount of P^{32} excreted in the urine and feces of normal individuals and patients, and to determine the effect on the blood and clinical findings of P^{32} given for treatment. Tables are presented showing the details of the results.

Greater concentrations of P^{32} are found in the blood and marrow when it is given intravenously than when it is given orally. The amounts retained by the different fractions of the blood varied in different cases but apparently the phosphorus finally reaches the stroma after passing through the hemoglobin fraction. But in general less than 1 per cent of the P^{32} retained by the red blood cells is found in the stroma.

The normal individuals excreted from 25 to 50 per cent of the P^{32} during the six days following its administration, no matter how it was given. The patients excreted less in both urine and feces than the normal individuals.

There was improvement in both the clinical and blood findings of the patients after the giving of therapeutic doses of radiophosphorus. —*Audrey G. Morgan.*

ERF, L. A., TUTTLE, L. W., and LAWRENCE, J. H. Clinical studies with the aid of radiophosphorus. IV. The retention in blood, the excretion and the therapeutic effect of radiophosphorus on patients with leukemia. *Ann. Int. Med.*, Sept., 1941, *15*, 487–543.

This article presents a study of 100 cases in which the rate of absorption and excretion of radiophosphorus is considered and its therapeutic effect in patients with lymphatic and myeloid leukemia is shown. Tables are given showing the details of the findings with regard both to absorption and excretion and to therapeutic action.

Radiophosphorus reaches nearly every cell in the body and concentrates in cells with active rates of metabolism. It is retained in greater concentration by circulating leukemic cells than by normal circulating white blood cells. For the first forty-eight hours after it is given, normal individuals excrete radiophosphorus more rapidly than patients with leukemia. The rates after forty-eight hours are about the same in the two groups of cases. Excretion goes on doubtless until all of the radiophosphorus has been excreted.

Radiophosphorus can be given in any way without damage to normal tissues. In these cases it was given orally and intravenously. It is well tolerated by both animals and human beings, and does not cause radiation sickness. It seems to bring about a marked increase of appetite for a few hours after its administration.

The authors found that the frequent administration of small doses (0.5 to 2 mc.) of radiophosphorus to patients with leukemia was better than larger doses at longer intervals. The results as shown by the tables are good enough to justify further use of the method. In 2 cases there was practically complete remission for two years, which is longer than has been reported with other methods of treatment. Both of these patients were still alive when the article was written. It is unfortunate that the lengths of partial and complete remission in all cases treated by various methods have not been recorded in the literature.—*Audrey G. Morgan.*

K'O, Y. K., TU, C. L., and CHAN, B. C. The effect of hard roentgen-rays on intestines of normal dogs fed on inorganic iron compounds. *Surg., Gynec. & Obst.*, Sept., 1941, *73*, 333–340.

Most patients who come for treatment for gynecological cancer show moderate to severe anemia resulting from repeated hemorrhages. Inorganic iron compounds would be good treatment for such anemias, but it seemed possible that the secondary irradiation from the iron particles might injure the intestinal mucosa.

Experiments were performed on dogs to determine whether such was the case. The conditions were made as nearly as possible like those in human beings. Normal dogs were given abdominal irradiation up to a total dose of 2,400 r

without other treatment. They did not show any clinical symptoms or pathological lesions in the small intestine at the end of treatment. Other dogs were given daily doses of ferrous sulphate or ferric ammonium citrate during the irradiation.

The giving of these drugs increased the hemoglobin content of the blood. Neither of the drugs caused any clinical signs of intoxication. Histological examination of the small intestine of the dogs treated with ferrous sulphate showed mild edema and congestion of the mucosa which disappeared completely in eight weeks. In the dogs treated with ferric ammonium citrate there was a greater degree of edema and large hemorrhagic areas in the mucosa. The severe hemorrhagic lesions persisted for more than eight weeks.

The experiments show that ferrous sulphate is valuable in the treatment of anemia from chronic loss of blood and does not injure the small intestine if given during irradiation, while ferric ammonium citrate does irritate the intestinal mucosa and is not to be recommended.—*Audrey G. Morgan.*

Speert, Harold. Cyclic changes in the mammary gland of the Rhesus monkey; preliminary report. *Surg., Gynec. & Obst.*, 1941, *73*, 388–390.

Attempts have been made to study cyclic changes in the human mammary gland but they have met with considerable difficulty and the reports are contradictory. Such a study of the mammary gland of the rhesus monkey is easier as the gland is smaller and more uniform in structure.

Histological study of biopsy specimens of 9 monkeys at different stages of the menstrual cycle have shown that there are definite changes dependent on ovulation. The characteristic changes are enlargement and increased vascularity of the lobules beginning seven to ten days before menstruation, reaching their height at about the time of menstruation and regressing slowly afterward. They occur only in the cycles in which ovulation has taken place.—*Audrey G. Morgan.*

Hoecker, Frank E. Evolution of the x-ray tube. *South. M. J.*, March, 1941, *34*, 280–284.

The gradual development of the roentgen tube from the discharge tubes used by Roentgen himself up to the Coolidge tube is described and illustrations given of types of tubes in use from 1897 up to 1915.

Physically a roentgen tube is an instrument which converts electrical energy into roentgen-ray energy when the charges, called cathode rays, strike a fixed object. In the earliest gas tube the charges were given off by a flat disc of metal enclosed in a partially evacuated glass bulb, and roentgen rays were produced when they struck the walls of the bulb. The images were fuzzy and blurred because of the large size of the source of the roentgen rays. The attempt to bring about greater clearness and detail and to produce tubes for therapeutic purposes led to increasing cooperation between physician and physicist. The gas in the early tubes was a necessary evil. The problem was to get rid of the gas without eliminating the stream of electrons, which was the essence of the process of generating roentgen rays. But Edison in 1883 found that electrons are evaporated from the surface of a metal when it is heated to a high temperature. This fact was first utilized practically by Fleming in 1905 when he made the first radio tube. In 1913 Coolidge applied it to the roentgen tube by replacing the concave cathode of the gas tube by a metal filament which could be heated by passing an electric current through it. This eliminated all the disadvantages of the gas tube and made it possible for designers of tubes to work out a multitude of special adaptations for specific purposes.—*Audrey G. Morgan.*

Hopwood, F. L. The irradiation of liquids. *Brit. J. Radiol.*, July, 1940, *13*, 221–226.

Since the discovery of neutron and positron in 1932 and of the method of artificial production of radioactive substances the next year much interest has been shown in studying the possible applications of these discoveries to the treatment of disease. In this Silvanus Thompson Memorial Lecture the author discusses and demonstrates experiments in treating proteins, organic and inorganic colloids, electrolytes and water with neutrons. He found that the effect of neutrons on these substances was of the same nature as that of beta rays or gamma rays but that neutrons are more effective than the gamma radium rays.

In irradiating solutions it was found that the primary action of the radiation is probably on the water rather than on the chemical compounds dissolved in it. If this proves true the

activation of water in the human body by irradiation during treatment will be found to be a significant factor in the results of treatment and possibly the predominant one.

It is possible that the chemical estimation of neutrons may prove an alternative to more familiar methods. Curves are given showing the details of the findings discussed.—*Audrey G. Morgan.*

MAYNEORD, W. V. Energy absorption. *Brit. J. Radiol.*, July, 1940, *13*, 235–247.

The author suggests that the effects of radiation depend, not so much on the dose at a particular point, as on the total energy absorbed in the body as a whole and discusses possible ways of determining its value. He also discusses the relationship of the roentgen to energy measurements and suggests the development of a unit which will include the estimation of such quantities as the total energy absorbed. The roentgen is known to be a measure of energy absorption in a given mass of air. He suggests the use of the gm.-roentgen indicating the energy conversion when a dose of 1 roentgen is delivered to 1 gm. of air and refers to the quantity obtained by integrating the dose throughout a given volume or mass as the "integral dose" throughout that region. He works out the formulae for the calculation of the integral doses in gm.-roentgens.

He says that at this stage little can be done except to suggest further investigation but it seems feasible to measure ultraviolet light and long wave length roentgen-ray flux in the common energy unit. Such a measurement would have great biological and practical interest. Such a method of measurment should also be extended to visible and infra-red radiation.—*Audrey G. Morgan.*

GRAY, L. H., and READ, JOHN. The neutron emission from a generator operating at 300 kV. *Brit. J. Radiol.*, July, 1940, *13*, 248–253.

In a previous paper the authors described an apparatus for the generation of neutron beams of sufficient intensity for biological research. The construction of the generator was supported by the British Empire Cancer Campaign. In this paper they describe three different methods for measuring the neutron emission from this generator: (1) reduction to thermal neutrons and measurement of the radioactivity induced by these neutrons in rhodium; (2) measurement of the intensity of gamma rays emitted when the neutrons of thermal energy combine with protons to form deuterium nuclei, and (3) measurement of the ionization produced by the fast neutron beam in air.

Tables are given showing the details of the results. They show that the agreement between the results of the three methods was satisfactory. The output of the generator is at present equivalent to about 30 curies of radon and beryllium. The energy absorption in tissues at the nearest point to the target at which biological material may be placed is, under good working conditions, about equal to that due to 2 r/min. of gamma radiation.—*Audrey G. Morgan.*

HAPPEY, FRANK. A portable "back-scatter phantom" for X-ray measurements. *Brit. J. Radiol.*, July, 1940, *13*, 254.

The portable back-scatter phantom described is used in conjunction with a Hammer dosemeter for the measurement of roentgen-ray dosage. A photograph is given showing the method of setting up the apparatus for surface dose measurements. This apparatus was introduced to replace the water phantom previously used, as the latter was cumbersome and great care had to be taken to keep water out of the ionization chamber, while this phantom has proved very light and easy to handle. The material used for producing back-scatter is masonite presswood which has the same specific gravity as water and similar scattering properties.—*Audrey G. Morgan.*